American Journal of Obstetrics and Gynecology

VOL. 57 MAY, 1949 No. 5

Original Communications

THE LOWER UTERINE SEGMENT*

Its Derivation and Physiologic Behavior

D. N. DANFORTH, PH.D., M.D., EVANSTON, ILL., AND
A. C. IVY, PH.D., M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology, Northwestern University Medical School, Chicago, and the Evanston Hospital; and the Department of Clinical Science, University of Illinois College of Medicine)

IN ALL natural phenomena the principles from which we start, like the conclusions which we reach, embody only relative truths. The experimenter's stumbling block, then, consists in thinking that he knows what he does not know, and in taking for absolute, truths that are only relative.''[1] In the case of the lower uterine segment, one must recognize that he deals only with working hypotheses rather than established facts, and that as new information is made available the hypothesis must be altered to conform with it.

In a previous article,[2] it was shown that the so-called ''isthmus uteri'' of the nonpregnant uterus is a variable segment whose boundaries are poorly defined and whose intrinsic structure does not differ significantly from the remainder of the corpus. It was also shown that during pregnancy the changes which occur in the isthmus are similar qualitatively and quantitatively to those of the remainder of the uterine musculature. Further, in the uterus through the fifth month of pregnancy it was not possible to distinguish the point of junction of the isthmic segment with the remainder of the corpus. In an earlier study of the Rhesus uterus during labor,[3] the findings suggested that the portion corresponding to the lower uterine segment, instead of elongating during the first and second stages of labor as it is commonly believed to do, actually underwent longitudinal shortening. Since our present understanding of the lower uterine segment is incompatible with these observations, certain changes must be made in order that the concept may conform to the findings. It is the purpose of this paper to present a working hypothesis which includes the factual observations and deletes certain of the inferences which are not based directly upon fact.

The historical aspects of the literature dealing with the lower uterine segment, and also the key articles, have been summarized by Stander,[4] and need not

*Presented before the Chicago Gynecological Society, Feb. 20, 1948.

be repeated here. It suffices to mention that, since the introduction of the term by Bandl in 1875, there is no single subject in the field of obstetrics which has been the source of as huge a literature. It was not until the concept of the isthmus uteri was introduced by Aschoff in 1905 that tacit agreement was reached as to the origin and boundaries of the lower uterine segment. The thesis of Aschoff was accepted in its entirety, and extended by Stieve. From this basis has developed our present understanding of the lower uterine segment.

I. The Present Concept

The classical concept of the lower uterine segment is difficult to summarize in specific terms since the structure is so variously interpreted. However, it is possible to outline certain fundamental features upon which most are agreed. According to present understanding, the lower uterine segment takes its origin specifically from the isthmus uteri of Aschoff. It will be recalled that the isthmus of the nonpregnant uterus, according to original definition, is a structure from 6 to 10 mm. long interpolated between cervix and corpus, bounded superiorly by the constriction in the lumen known as the anatomic internal os, and inferiorly by the point of transition from endocervical to isthmic type of mucosa, the histologic internal os. Stieve and Aschoff have reported lengthening of this segment in early pregnancy,[2] and dilatation down to the level of the histologic internal os so that the isthmic wall comes to form, together with the corpus, part of the wall of the ovum chamber. The site of the obliterated anatomic internal os is said to be marked by a ledge or thickening of the musculature which has been designated as the physiologic retraction ring.[5] This ring remains until the termination of pregnancy, dividing the uterine cavity into two portions which are designated as the upper uterine segment and the lower uterine segment, respectively. Upon the basis of evidence both from frozen sections at term and examination of the uterus at the time of elective cesarean section, it has been shown that the region of the lower segment is thinner than that of the upper, and that the transition between the two is often abrupt. It is shown further that during labor there is progressive thinning of the lower uterine segment in contradistinction to the thickening which occurs in the upper, and that, in the presence of neglected obstructed labor, uterine rupture occurs through this attenuated lower segment. Because of the latter finding, together with other evidence which is not clear to the writers, the lower uterine segment is believed to be passive in labor, in contrast to the upper portion which performs the active work of parturition. The thinning of the lower pole is assumed to occur as the result of longitudinal stretching of this segment, the evidence for this being the gradual elevation of the physiologic retraction ring on the abdomen as the corpus thickens.

Certain descriptive terms have been coined to clarify the precise changes in the muscle fibers during these happenings.[5] Though slow of acceptance, they or some similar terms are essential to an adequate understanding of the uterine adjustments of labor. The term brachystasis was introduced to describe the changes in the corpus, consisting of a progressive, ratchetlike thickening in this segment with successive pains. It connotes a cycle of contraction of a single muscle fiber, during which the fiber first contracts, and then relaxes to a shorter length than before the contraction but at this shorter length it manifests the same tension as it did prior to contraction. By a series of such contractions the fiber becomes progressively shorter, but in its relaxed phase, despite this shortening, its relaxed tension is not altered. By envisioning the entire musculature of the upper segment contracting in this wise, one can readily understand the progressive thickening and shortening which occurs in this segment. The converse of brachystasis is mecystasis, which connotes an interval fixation at greater

length, at which greater length the fiber manifests the same tension as it did prior to contraction. Mecystasis is considered as occurring in the lower segment during the first stage of labor, since, according to present understanding, this segment undergoes both circumferential dilatation and longitudinal elongation, together with progressive thinning.

Before this theory may be modified, the inferences must be distinguished from the factual observations. The former may be deleted at will from any new hypothesis; the latter must necessarily be included and fully accounted for. The factual observations include the following:

A. Prior to the onset of labor the lower uterine segment is often thinner than the upper. The transition between the two is often abrupt, and, at this stage or in normal unobstructed labor, it is known as the "physiologic retraction ring."

B. The lower uterine segment becomes progressively thinner as labor advances.

C. The upper uterine segment becomes progressively thicker as labor advances.

D. In both normal and obstructed labor, the junction of the upper and lower uterine segments is increasingly distinct, and advances cephalad as labor continues.

E. In obstructed labor, uterine rupture occurs through the thinner lower uterine segment.

To these well-known observations, one may now add the following:

F. During the first half of pregnancy the point of junction of the upper and lower segments is not distinguishable. A physiologic retraction ring is not present until some time in the last half of pregnancy.

G. There is no intrinsic structural difference in the musculature of the upper and the lower poles of the uterus above the level of the cervix.

H. Study of the Rhesus uterus, which is similar in type to that of the human being, indicates that the lower pole of the uterus shortens progressively during the first and second stages of labor.

I. In normal labor, the lips of the cervix rise in the pelvis as dilatation proceeds. At full dilatation they reach the plane of the inlet, as is demonstrated by x-ray studies made with metal clips upon the anterior and posterior lips.[6]

The hypotheses which may be deleted, since they are not based upon observation are the following:

A. That the lower uterine segment takes its origin specifically from the isthmus uteri of Aschoff. Recent work has shown that the isthmic segment is subject to much variation and cannot be considered as a discrete and clearly defined anatomic entity. If these observations are accepted, then the isthmic segment should be viewed as an indefinite, variable portion of the lower pole of the corporeal musculature; and one may not correctly assume that the lower segment comes specifically and solely from the isthmus uteri of Aschoff.

B. That the lower uterine segment is a passive structure in labor. It has been shown that the musculature of the lower segment is anatomically similar to that of the upper segment, with two exceptions which are considered as not relevant to this discussion (these are an abundance of sensory nerve endings in the lower pole of the uterus, and also a greater amount of elastic tissue). Since the lower segment is a muscular structure, there is no reason to suppose that it would not contract to the best of its ability, just as does the upper segment. Also, the demonstration that this portion shortens in the Rhesus uterus during the first stage suggests that, indeed, it is quite as active as the upper portion of the uterus.

II. A Suggested Hypothesis

The Derivation and Boundaries of the Lower Uterine Segment.—

It has been shown elsewhere,[2] and recently confirmed,[7] that the cervix is basically a fibrous structure. In considering the contractile function of the uterus, it is, therefore, necessary that this portion be distinguished from the muscularis; and it is considered proper that the inferior boundary of the lower uterine segment be located at the fibromuscular junction of cervix with corpus.

The delineation of the superior border of the lower uterine segment is less obvious. It may be stated unequivocally that a specific point of junction of upper and lower segments cannot be distinguished in the uterus up to the fifth month of pregnancy. One, therefore, infers that the lower uterine segment does not develop into a definitive, clearly evident structure until later. Since the

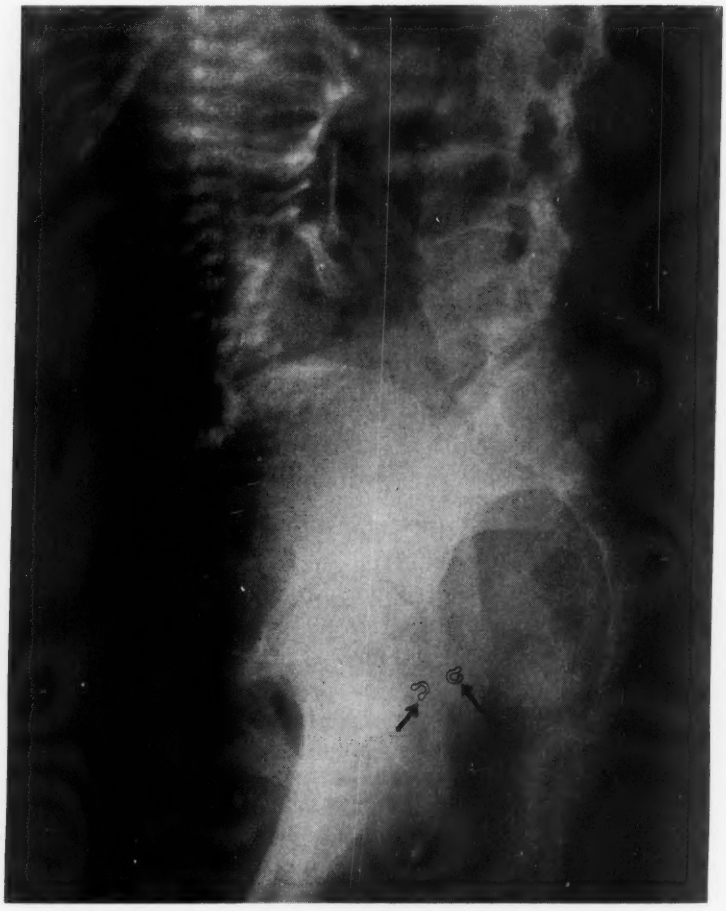


Fig. 1.—Lateral x-ray, metal clips on cervix. Early first stage of labor.

lower pole of the uterus (excluding the cervix) is roughly cup-shaped, it is apparent that there is a point along the uterine wall below which circumferential dilatation must occur in order for the baby to pass, and above which the diameter is already great enough that no such further dilatation need occur. It is considered that this point marks the junction of the lower and upper uterine segments, and that the level at which this point occurs in any given uterus is determined only by the relationship between the size of the presenting part and its level in the uterine cavity. In accordance with this thesis, one may define the lower uterine segment as the portion of the uterine musculature which must

undergo circumferential dilatation. It is considered that this differentiation may begin either in early labor, or in the uterine adjustments which immediately precede labor (Fig. 3).

The Physiologic Behavior of the Lower Uterine Segment During Labor.—

The evidence which is available suggests that brachystasis occurs not only in the upper uterine segment, but rather that it is a fundamental property of pregnant uterine muscle, occurring throughout the entire musculature. As this occurs in the lower segment proportionately to that in the upper, this area is necessarily dilated as it pulls up about the presenting part. And thinning is a necessary accompaniment to this circumferential dilatation of the lower pole of the uterus. Longitudinal shortening of the lower uterine segment, with consequent dilatation and thinning, are considered to proceed gradually, progressively, from above downward, until ultimately the cervix itself is involved and

Fig. 2.—Same patient as Fig. 1. Late second stage.

full dilatation of the cervix is reached. Given a normal circumstance, at this stage one finds the upper uterine segment thickened by brachystasis, and also shortened in the same process; the lower uterine segment shortened by brachystasis but thinner because of circumferential dilatation; and the cervical lips at about the level of the inlet (Fig. 4). This stage is beautifully shown in Eastman's recent sagittal section,[8] illustrated in Fig. 6.

If at this time there were no obstruction whatever to the passage of the baby, delivery could be accomplished by gravity merely by placing the patient in the erect posture. Even in entirely normal labors, however, some moderate obstruction is offered by the maternal soft parts and the bony pelvis. This must

be overcome by the force of uterine contractions pulling against the now-taut uterine supports, these being the sites upon which the uterus gains its purchase. (Mengert[9] has shown that of these supports the transverse cervical ligaments are the most important, the pubocervical fascia and the uterosacral ligaments less so.) Further changes in the uterus are considered as being wholly dependent upon the amount of effort which is expended by the uterus in overcoming the

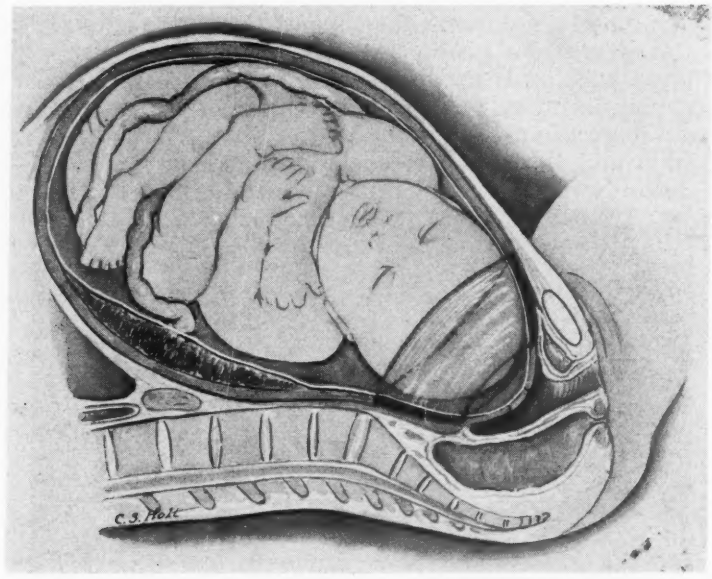


Fig. 3.

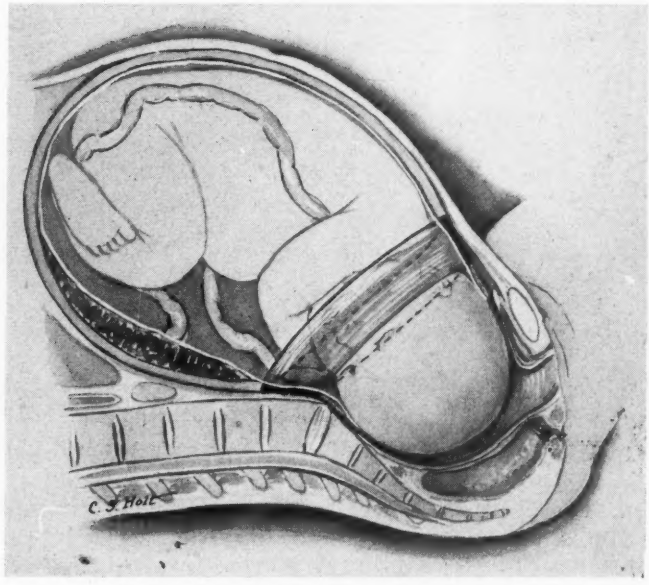


Fig. 4.

obstruction which is offered. If the obstruction is negligible, one would expect the uterus to shorten as a whole and empty itself. If there is significant obstruction to be overcome, however, such that advancement with each contraction is disproportionate to the attempt at progressive shortening which occurs in the

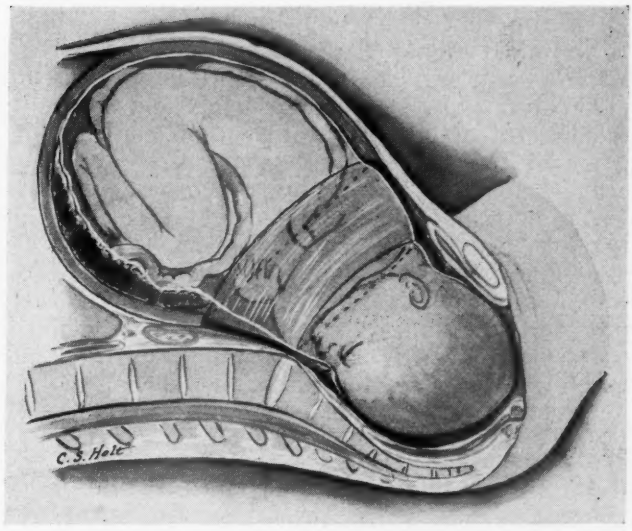


Fig. 5.

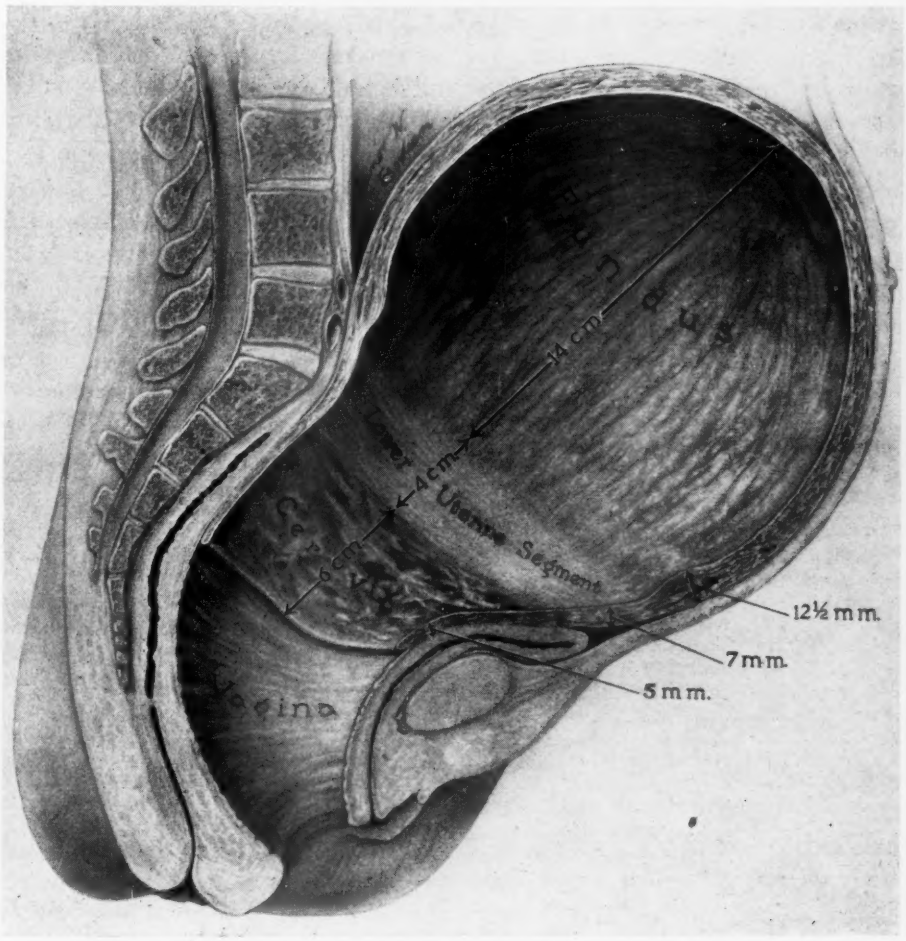


Fig. 6.—(From Obstetrical and Gynecological Survey. Williams and Wilkins Company, Baltimore. Courtesy of Dr. N. J. Eastman.)

uterine muscle, it is apparent that certain uterine adjustments must result. If the cervix could be pulled higher in the pelvis with successive pains, it is suggested that upper and lower segments would continue to shorten proportionately. However, since the cervix can go no higher, being held by the taut uterine supports, and since powerful brachystatic contractions continue, it is evident that the weakest portion of the uterine musculature must give way. The weakest portion, as mentioned above, is the portion which has been excessively thinned by circumferential dilatation. It is suggested that at this time only does elongation occur in the lower uterine segment (Fig. 5), that is, in the presence of significant uterine effort in the second stage of labor in the face of obstruction, either relative or absolute. It is suggested further that the early phases of this elongation may be through a mecystatic mechanism, as defined above. If the disproportion is not overcome and labor continues, uterine rupture must necessarily occur through the elongating lower uterine segment.

Summary

The present concept of the lower uterine segment is briefly reviewed. Revision of this concept is made necessary by certain recent work, the essential features of which are outlined.

To conform to these observations, it is suggested that the inferior border of the lower uterine segment be placed at the fibromuscular junction of cervix with corpus. It is considered that the superior border of the lower uterine segment occurs at the point along the uterine wall below which the uterus must dilate in order to allow the baby to pass. The lower uterine segment, therefore, is defined as the portion of the uterine musculature which must undergo circumferential dilatation during labor, its extent being dependent upon the size of the presenting part and its level in the uterine cavity. The available evidence suggests that brachystasis, with retraction, occurs in this segment just as it does in the upper, and that thinning in the first stage of labor is due not to passive elongation, but rather to active shortening of the cup-shaped lower pole with dilatation as it is pulled up about the presenting part.

It is believed that under normal circumstances, longitudinal elongation of the lower uterine segment occurs only during the second stage of labor when there is significant obstruction to be overcome.

References

1. Bernard, Claude: An Introduction to the Study of Experimental Medicine. Translated by H. C. Greene, New York, 1927, The Macmillan Co.
2. Danforth, D. N.: Am. J. Obst. and Gynec. **53**: 541, 1947.
3. Danforth, D. N., Graham, R. J., and Ivy, A. C.: Surg., Gynec. & Obst. **74**: 188, 1942.
4. Stander, H. J.: Textbook of Obstetrics, New York, 1945, D. Appleton-Century Co., p. 295.
5. Ivy, A. C., and Rudolph, L.: Surg., Gynec. & Obst. **67**: 188, 1938.
6. Stillman, James, and Caldwell, W. E.: Unpublished data.
7. Schwarz, O. H., and Woolf, R. B.: Am. J. Obst. & Gynec. **55**: 151, 1948.
8. Eastman, N. J.: Obst. & Gynec. Survey **1**: 651, 1946.
9. Mengert, W. F.: Am. J. Obst. & Gynec. **31**: 775, 1936.

Discussion

DR. FREDERICK H. FALLS.—The work here presented must be considered as an attempt to explain the very interesting clinical phenomena which appear in the pregnant uterus, especially in the region of its lower pole during pregnancy and labor. As pointed out by Dr. Danforth, the last word has not been said previously and certainly not tonight. However, if we do not talk about, speculate on, and experimentally observe these clinical phenomena, we never will advance our knowledge concerning them.

I think we will all agree with the writers that the lower uterine segment cannot be a passive structure as has been contended by some. Where else in nature are found muscle cells that do not contract? One cannot argue from this, however, that it is the contractions of the lower uterine segment fibers that are the principal factors in the dilatation of the cervix and its upward retraction. The downward push of the uterus on the presenting part would seem to be more logical explanation, causing a wedge like opening of the cervix and lower fibers of the lower uterine segment. There is a small but very important group of cases for this discussion, in which the fibers of the lower uterine segment are elongated to such an extent that the clinical appearance leads one to believe that the woman has a full bladder. The first time I saw this phenomenon in a woman in labor I was curious as to the behavior of this part of the uterus after the pains became strong. Fearing rupture, I stayed in continuous attendance on the case. Labor progressed in a perfectly normal manner and spontaneous delivery resulted. There was no tenderness of the lower uterine segment, in spite of the obvious elongation of its fibers and the height of the ring marking the junction of the lower and upper uterine segments, and no other clinical sign of threatened rupture of the uterus.

Another clinical fact that I should like to point out is the difference between the ring at the junction of the upper and lower uterine segment and the muscle either above or below during labor. The best way to appreciate this is to put one's hand into a uterus that is contracting in a case of dystocia. When the hand is in the lower uterine segment there is very little compression. When an attempt is made to pass the constriction ring, the muscle is found to be in continuous tetanic spasm and as hard as a steel band. Above this, the uterine muscle is contracting and relaxing rhythmically but futilely because of spasm of the ring. Here, then, is a continuous spasm of one part of the upper uterine segment and a contraction and relaxation of another part.

I am not convinced of the appearance of brachystasis during labor. If this were so, then there would be a continuous thickening of the whole upper uterine segment during labor. In doing a number of classical cesarean sections, I have not been impressed by the fact that the upper uterine segments of those in labor were thicker than those not in labor, even when the operation was done under local anesthesia, which would obviate the possibility of the anesthetic agent's causing secondary relaxation of the brachystasic contraction.

We have a specimen confirming Dr. Danforth's observation that the lower uterine segment does not form until the latter months of pregnancy. I removed a five months' pregnant uterus in a girl with active tuberculosis at the insistence of the medical department because of a rapidly progressive pulmonary tuberculosis. I hardened this specimen in formalin before opening and measured the thickness of the uterine wall. There was no contraction ring noted and very little difference between the upper and lower uterine segments.

DR. M. EDWARD DAVIS.—The derivation and the physiologic behavior of the lower uterine segment has been of more than academic interest for very many years. The changes incidental to the development of the uterus for parturition are of fundamental importance in order to understand the mechanism of labor and delivery. However, as the authors point out, there is considerable difference of opinion concerning these basic changes.

The uterus must differentiate into three distinct parts in order that delivery can be accomplished. The long, closed cervix must be slowly converted into a thin-walled passageway which connects the corpus and the vagina and plays a passive role during labor. The structure of the cervix lends itself to this role, for, as Danforth has pointed out in a previous communication, it consists of fibrous tissue without muscle cells.

The corpus of the uterus is differentiated into an upper and a lower segment. The upper segment with its thick muscular wall is the actively motile portion. It provides the activity necessary to alter the lower segment as well as to convert the cervix into a passive canal by the process of effacement and dilatation. The lower segment, largely muscular but containing much elastic tissue, has a fixed inferior border at the fibromuscular junction with the cervix and corpus. Its superior border, however, varies considerably, depending on many factors such as the length of the pregnancy, the parity of the patient, the length of labor, the degree of obstruction to be overcome, and the size of the baby. It must likewise provide sufficient room to allow the baby to pass through its lumen.

This concept presented by the authors is supported by much sound experimental data. However, many clinical observations must be reconciled with it. The lower uterine segment

has its origin in the last trimester of pregnancy and may be of sufficient length to admit the passage of a baby through it at cesarean section, long before the end of pregnancy. Does this signify that the separation of the uterine corpus into upper and lower segments is a growth process, the accompaniment of the developing pregnancy? Although the lower segment has some contractility, its motility in labor does not compare with the upper segment. Following the delivery of the baby at cesarean section, the walls of the lower segment remain flabby and thin whereas the upper segment promptly thickens. If the lower segment contracted actively in labor, would it not exhibit more muscular tone at this time? We have assumed that the low cesarean section was carried out in the lower uterine segment. Is it probable that the incision extends into the cervix and that it is not limited to the lower uterine segment? One other clinical observation that troubles me is the effacement of the cervix. As the internal os disappears and more and more of the cervical canal becomes obliterated, what effect do these changes have on the lower uterine segment? These are a few of the questions which this excellent presentation has raised in my mind. No doubt further work will fit our clinical experiences into these new basic concepts.

DR. A. C. IVY.—Some of the remarks made by the discussers reminded me of the reason I became interested in the subject of the physiology of the uterus. Dr. Rudolph came to me many years ago and told me about a case of obliquity of the uterus, which indicated to me that the uterine musculature manifested physiologic properties and a coordination of parts analogous to the heart and stomach, and that certain motor abnormalities must be due to a disturbance of the coordinating mechanism and contractility of the uterine musculature. For example, when Dr. Falls mentioned the elongation of the softened lower pole of the uterus which he has observed, to me that can only be explained by a physiologic loss of tone in the lower portion of the uterine musculature which we commonly refer to as the lower uterine segment. The contraction of one half of the body of the uterus more vigorously than the other half will cause obliquity.

When one stops to consider the question, how is it possible for labor to make any progress, for dilatation and effacement and descent to occur without brachystasis, we are forced to the conclusion that brachystasis of the longitudinal musculature is a sine qua non for these processes. It simply has to occur, and there is no other way to explain progress. Thickening of the shortened muscle has to take place.

As is true for all physiologic processes, we should not expect the process of labor to be stereotyped. We should not expect it to occur exactly the same way every time. In order to obtain an acceptable view of the normal variations of the behavior of the uterus in labor, we need more evidence from frozen sections such as submitted more recently by Dr. Eastman. We need more information of the type submitted by Dr. Danforth. It is with evidence of this sort that we shall resolve in the course of time the differences of opinion relative to the physiologic anatomy of the uterus in pregnancy and labor.

I believe the evidence that has been assembled by Dr. Danforth emphasizes the fact that, prior to the development of the physiologic retraction ring, no one can put his finger on the wall of the uterus and state that this is the junction of the upper and lower segments. The concept of the junction submitted by Dr. Danforth provides a new way of defining the junction. I suspect, when all the evidence is in, we shall find that the junction and the physiologic retraction ring are identical.

We need such evidence as follows to support the relationship of what we conceive to be the site of junction of the upper and lower segments and the anatomic internal os. When the occasion arises that the uterus has been exposed and the physiologic retraction ring has been seen and measured, some nonabsorbable, preferably opaque material should be inserted so as to label the retraction ring, preferably at three points, right, left, and anteriorly. Then, if, on making an x-ray or an anatomic examination, it is found that the nonabsorbable material is located at the level of the anatomic internal os, the question would be settled. It would be better, of course, if a case were at hand in which later a hysterectomy would be indicated so that the specimen could be examined anatomically. We have such evidence for the monkey and there is no good reason why the uterus of the monkey should differ significantly from the human uterus.

The upper and lower segments of the uterus are physiologic as well as anatomic parts of the uterus. The fact is, the lower segment is not passive, as Dr. Falls properly emphasized. It is contracted, or, in other words, resists stretch; and if it were not contracted it would not resist stretch and it would balloon out. Even though the lower segment is an active segment, it is relatively passive when compared to the upper segment. The musculature of both segments contracts and manifests changes in length and tension.

DR. LOUIS RUDOLPH.—It is rather unfortunate that the word "ring" was ever added to this junction. The second stage frozen section of Braune shows a definite ring. The second stage sections of Chiara show a tapering of the thickened upper segment into the thinned lower segment. The junction of the upper and the lower uterine segments is just a tapering of one segment into the other in the region of the fixed anterior uterine peritoneum. Some years tgo I wrote to one hundred and four leading obstetricians, inquiring if they had seen or felt a ring during the performance of cesarean section. The answers were in the negative.

The brachystasis is manifested mainly in the fundus uteri of the upper uterine segment and then tapers downwards into the lower uterine segment. According to Aschoff the junction of the upper and the lower uterine segments, or the physiologic retraction ring, is in the region of the anatomic internal os. An intrauterine examination after the delivery of the placenta presents a firm thickened upper segment and a flaccid lower segment, the junction of which is abrupt, due to the 3 to 4 cm. thickening of the upper segment and a thinned lower segment which is about 1 cm. thick. This junction is not a ring, but, as Barbour described it, a ledge, ridge, or a rim between the two segments.

The next point I want to dwell upon is the cervix. Dr. Davis still has the idea that the cervix is opened or dilated purely by the mechanical factor of the upper uterine segment which pushes the presenting part through the cervix. If we study parturition in the dog, we have a beautiful example of what nature does. With the fingers in the cervix after a pup is born, the cervix remains relaxed until the next pup descends to dilate the cervix. The cervix is left relaxed for the oncoming pup.

Dr. Danforth has presented definite evidence of the fibrous nature of the cervix with muscular tissue in the main of 10 to 15 per cent, which I can substantiate. Recently we studied 40 postpartum patients to determine the return of normal topography of the cervix. Immediately after the delivery the cervix is thin, except the anterior lip which is about 4 to 5 cm. thick. On the third or fourth postpartum day, the postpartum cervix returns to its normal topography. Is this return due to fibrous tissue readjustment or do the small muscle elements play a role in its return to normal?

Does the fibrous tissue have a function? What is the physiology of the fibrous tissue? We know clinically that the "obstetric" internal os and the external os have a sphincteric function during a Braxton Hicks version and during the delivery of the fetal head in a breech labor. What is this physiology of the spasmodic condition of the "obstetric" internal os and the external os in view of the fact that the cervix is nearly wholly fibrous? The question is, how much muscle tissue is necessary in the fibrous cervix for sphincteric property?

When we think of brachytasis of the upper uterine segment, we must realize that the circular mecystasis or dilatation of the cervix is coordinated to anatomic changes of the upper uterine segment by brachystasis.

DR. DANFORTH (Closing).—May I emphasize again that the thesis which we have presented is an attempt to outline what would happen if labor were to proceed in an entirely "normal manner"? However, it is questionable whether any of us has ever seen such a labor, and if we did see one in the future, whether we should recognize it as such. In answer to Dr. Rudolph's question concerning the amount of muscle which is necessary for sphincteric function: in occasional cervices which are examined histologically with contrast stains, small accumulations of muscle tissue are found which conceivably might be capable of functioning as a sphincter. In the majority of cervices, however, muscle tissue is extremely sparse, amounting to perhaps 10 or 15 per cent of the total cervical tissue, and is diffusely scattered; it would seem extremely difficult to ascribe sphincteric possibilities to this muscle.

VASCULAR PATTERNS IN THE HUMAN OVARY*†

BARNET DELSON, B.S., M.D., SAMUEL LUBIN, M.D., F.A.C.S., BROOKLYN, N. Y., AND S. R. M. REYNOLDS, PH.D., BALTIMORE, MD.

(From the Department of Obstetrics and Gynecology, Cumberland Hospital, Brooklyn, N. Y., and the Department of Embryology, Carnegie Institution of Washington, Baltimore, Md.)

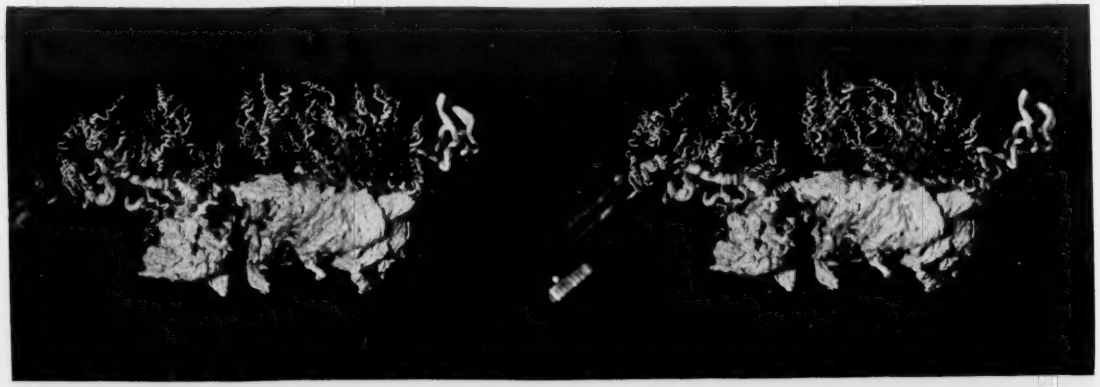
OVARIAN spiral arteries, long forgotten after their original description in the literature, have been rediscovered recently, and much concerning their nature and functions has been learned.[1] Instances may be cited from medical history illustrating a cycle of initial discovery of a fact, its passing into oblivion, and rediscovery at a later date. The latter may occur at a favorable time when newer data are available in allied branches of science sufficient to give the original observation an important meaning. One such example is that of the discovery of William Hunter in 1774[2] of the spiral arterioles in the human endometrium. In 1936, these were rediscovered by Daron[3] in the monkey, *Macacus rhesus*. By this time, knowledge of the physiology of the uterus was sufficiently advanced so that certain functions could be ascribed to endometrial spiral arterioles. A rather similar situation exists with respect to the spiral arteries in the ovary.

Farre[4] first made mention of spiral arteries in the human ovary in 1858. His description is most accurate but limited in scope, and the illustration in his article of their location and distribution in the ovary is inadequate. Belou[5] in 1934 presented stereoscopic radiographs of spiral-like arteries in the human ovary, and referred to them as balls of helical vessels. In 1947, it was observed[1] in the ovary of the rabbit that the arterial branches in the hilus of the ovary are spirals of gradually diminishing diameter. These lie along the length of the hilus of the ovary. In further studies,[6-8] it was shown that adaptive alterations occur in the spiral arteries when the ovary changes in size. When the size of the ovary was increased by injection of chorionic gonadotrophin into the rabbit, the helical spirals became extended, usually in an even, orderly fashion. In this way, they became adapted to the enlarged ovary. In addition to extension, lateral flattening of the coils also occurred. The effect is transient, since regression occurred following a decrease in ovarian size as stimulated follicles became atretic. Spiral configuration is restored largely by the sixth day following intravenous injection of the gonadotrophin, although flattening of the coil lasted as late as the ninth day. This is the effect of normal ovulation and luteinization. When corpus hemorrhagicum cysts occurred in the rabbit ovaries following injection of chorionic gonadotrophin, distortion of localized portions of the spiral artery was observed in the vicinity of these cysts. It was suggested that distortion of the spiral artery might contribute to cystic development through the mechanism of altered local hemodynamic relations in the ovary during the active growth phase of the follicle under stimulation of the gonadotrophins. This observation of an association between distortion and cysts suggested that spiral arteries in the ovary normally serve to regulate the local blood pressure within the ovary.

*Presented at a meeting of the Brooklyn Gynecological Society, April 2, 1948.
†Aided by grant from the Kate Lubin Research Foundation, Inc.

Fig. 1.—Vinylite cast of the main ovarian artery in human ovary that was grossly sclerotic. The patient was a 53-year-old woman, para ix, gravida x with a history of nephritis and diabetes mellitus for eight to ten years prior to death. Blood pressure 210/112. Menopause in 1943. Postmortem specimen. Ovarian artery injected. Note spiral configuration of cast of this main or primary ovarian artery at one point, whereas the remainder of the ovarian artery is irregular and undulant. The branches are sparse, thin, shortened, and widely spaced. Such branching appears to denote ovarian inactivity. Compare with Fig. 6. See Table I, A, no. 12. Stereoscopic view (×2).

Fig. 2.—Injection-corrosion preparation of ovarian arterial pattern from a patient with recent menopause and a proliferated endometrium. A 54-year-old woman, para i, gravida vii, with past history of breast carcinoma and tumor of uterus. Blood pressure of 138/60. Last menstrual period 1945. Surgical specimen. Hysterectomy with bilateral salpingo-oophorectomy (fibroid uterus). The ovaries were grossly sclerotic. Uterine arteries injected. Note the characteristics of branching with parallel appearance of branches as they proceed to periphery of ovary. Compare with Fig. 3, where branching is more profuse, and with Fig. 1, where branches are sparse and small. The dense mass of plastic lying over the middle of the main ovarian artery and extending downward is an artifact caused by plastic that escaped from a ruptured vessel. See Table I, B, no. 23. Stereoscopic view (×1½).



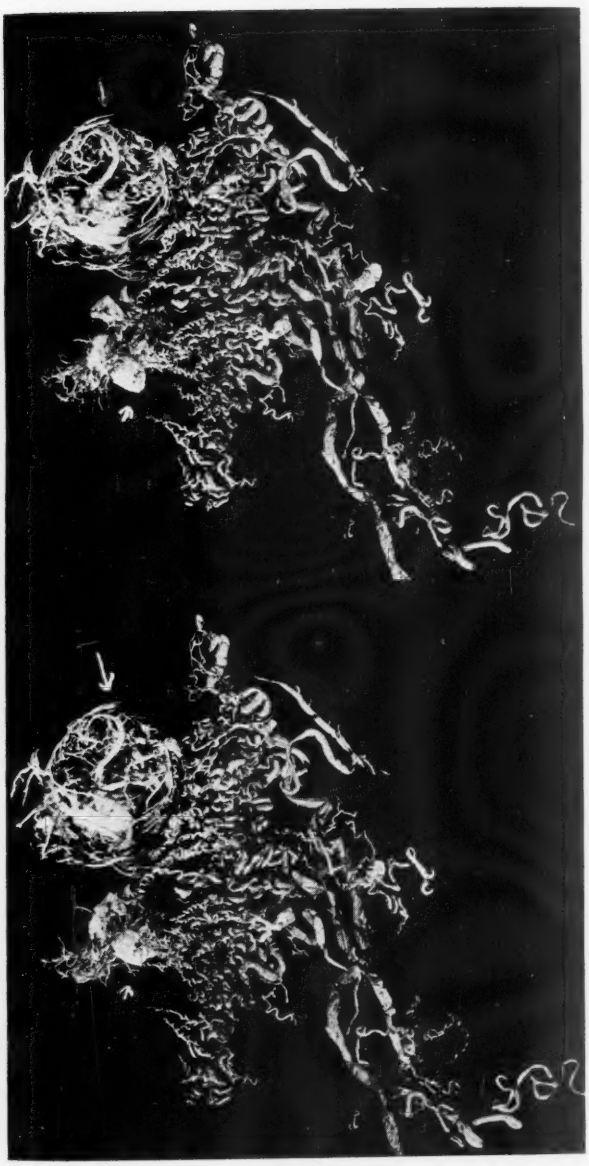


Fig. 3.—Injection-corrosion preparation of a cast of the ovarian arteries from a patient menstruating regularly at the time of operation. A 35-year-old woman, para ii, gravida iii, having a fibroid uterus. Blood pressure 110/80. Menstruating regularly. Surgical specimen. Hysterectomy and bilateral salpingo-oophorectomy. Uterine artery injected. Note especially the profuse arterial branching, extreme crowding of the arteries and the large, loosely woven body to the right which is the cast of the blood vessels of a corpus luteum (large arrow). The small structure to the left (small arrow) is a follicular cyst which was injected. Extended tertiary spiral arteries can be seen in the vicinity of the corpus luteum and cyst. Compare with Fig. 2 and Fig. 1. Stereoscopic view (×1½).

In the present work, the patterns and distribution of the ovarian spiral arteries in the human ovary were studied in order to ascertain the extent to which the conditions observed in the rabbit apply to the human. Following a modification of the technique originally employed, surgical and postmortem specimens of human ovaries were injected with vinylite plastic (vinyl acetate), and the vascular tree was subsequently isolated following the use of a corrosion bath.[9]

Technique

An 18-gauge hypodermic needle with blunted tip was inserted into the vessel to be injected. In some cases injection was made through the ovarian artery, and in others the uterine arteries were used. Equally good casts were obtained either way because of the free inosculation to which Farre refers, which exists between the uterine and ovarian arteries.[4] The other arterial stump, uterine or ovarian, as the case might be, was clamped. In infant and fetal specimens, injection was made by way of the lower aorta. The tissues around the vessel were tied securely with a ligature.

A small amount of acetone was injected in order to prevent a premature hardening of the plastic. Colored vinylite solution was then injected as rapidly as possible. A time interval of fifteen minutes was permitted to elapse so that adequate hardening could take place. Following this the injected ovary was trimmed away from the surrounding tissue and placed in a corrosion bath, which consisted of 500 c.c. of water, 5 c.c. of hydrochloric acid, and one-fourth to one-half teaspoonful of pepsin. This bath was incubated at 37° C. The vascular casts were digested free of tissue in ten to fifteen days. In preparations from the fetus, however, only twenty-four hours were required for complete digestion to take place. Small adherent bits of tissue were readily washed away from the cast under a gentle stream of tap water or by careful rotation in a beaker of water. Thus far, sixty sets of ovaries have been prepared and carefully studied.

Results

Normal Adult Ovary.—The main ovarian artery as it courses in the hilus of the ovary is noted to be undulant, tortuous, with a degree of flattening. In only one case was there a regularly formed spiral for a short distance (Fig. 1). The branches of the main ovarian artery proceed from the hilus into the ovary in a parallel manner reminiscent of the teeth of a rake (Fig. 2). In an actively functioning ovary, or one containing many structures, such as cysts or corpora lutea, this configuration may seem obscure, but close examination reveals its presence. The basic pattern is best seen in inactive ovaries or in those less active or those beginning to undergo involution. In such cases the branching is not so profuse and hence does not confuse the appearance of the basic arterial pattern (compare Figs. 2 and 3).

Primary, secondary, and tertiary branches are noted arising from the main artery in the hilus. The primary trunks are usually tortuous or undulant with an occasional spiral. They are also usually flattened. The degree of crowding together among the various branches is dependent upon the presence and size of specialized structures in the ovary, such as cysts and corpora lutea. The space is also affected by the altered activity of the ovary, as in the menopause, and probably also by the size of the underlying veins in the pampiniform plexus (Figs. 1, 3, 4, and 5). Arising from the primary trunks are the secondary branches. These are smaller in diameter and show essentially the same characteristics as found in the primary branches. However, a greater tendency to spiralling is noted in the smaller vessels. The tertiary branches arising from

the secondary arterial branches are the smallest arteries demonstrated. From these the small arterioles and eventually the capillaries arise. These tertiary vessels regularly show the greatest spiralling.

Spiralling in all branches, but particularly in the tertiary vessels, occurs in the form of a helix with a gradually diminishing diameter. It proceeds in a counter-clockwise direction as originally observed in the rabbit.[1] The tightness or compactness of the spiral is influenced by the presence or absence of pathology, by the presence of cysts, large Graafian follicles or corpora lutea, by the menopause, and apparently also by engorgement of the venous system of the ovary.

Evidence that an extension of the spirals and some flattening of the ovarian spiral arteries occurs in relation to the presence of localized structures within the ovary (follicles, corpora lutea, and cysts) has been observed, and will be described in a future publication.

In rabbits an orderly sequence of extension and regression of the spiral arteries was demonstrated following injection of gonadotrophins.[6, 7] This, of course, could not be done in the human beings.

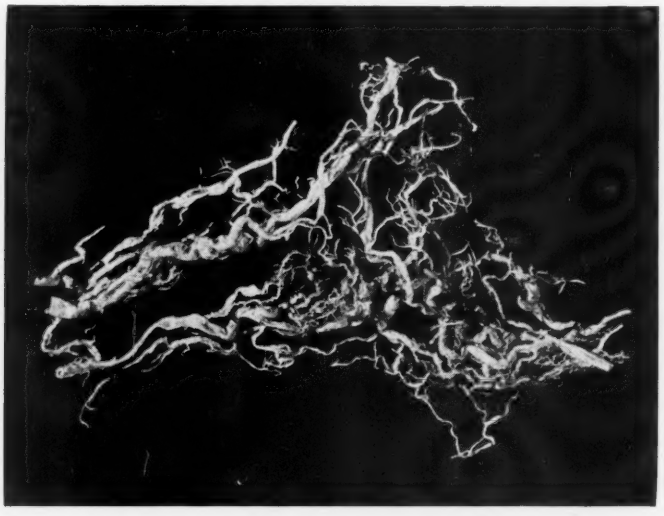


Fig. 4.—An injection-corrosion preparation of the veins in the ovary from a regularly menstruating subject. A 39-year-old woman, para ii, gravida ii, with past history of hypertension and kidney disease. Blood pressure 170/100. Postmortem specimen. Ovarian vein injected. Note especially the venous configuration, the pampiniform plexus, the tortuosity, irregularity, flattening, anastomosis and the absence of spiralling. Compare with arterial casts and with Fig. 5. Observe how difference in thickness and density of the plexus may affect crowding of arteries (×8).

Abnormal Adult Ovary.—Early in this work an arterial cast of a 53-year-old woman with diabetes, nephritis, and hypertension of many years' standing was obtained. The patient had not menstruated since 1943. It was remarkable to observe the unusual appearance of the arterial branches coming off the main ovarian artery. These were observed to be sparse, broadly-spaced, thin, and shortened. In fact, the vessels appeared to indicate marked inactivity, as compared to the luxuriant branching noted in ovaries of a younger group of patients in the reproductive period of life (Fig. 1). These branches were lying close to the main ovarian artery. There was only a slight amount of spiralling present (compare Figs. 1 and 3).

A similar configuration to the above was noted in three other specimens (see Fig. 6). The patients from whom these preparations were made had in common: (1) age; they were in the fifth decade of life or over; (2) hypertension; (3)

Fig. 5.—Injection-corrosion preparation of the venous network from a patient with a history of menometrorrhagia and fibroid uterus. Subject was a 34-year-old multiparous woman. Blood pressure 130/80. Total hysterectomy and bilateral salpingo-oophorectomy. Uterine vein injected. Compare with Fig. 4 (×2).

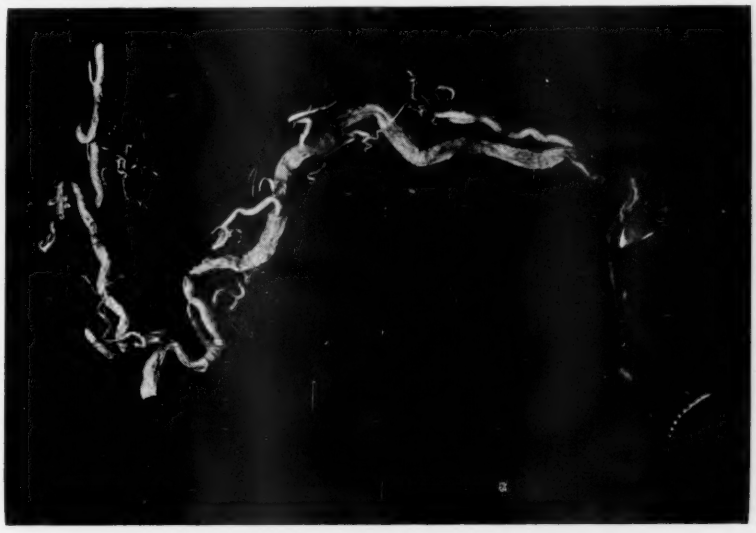
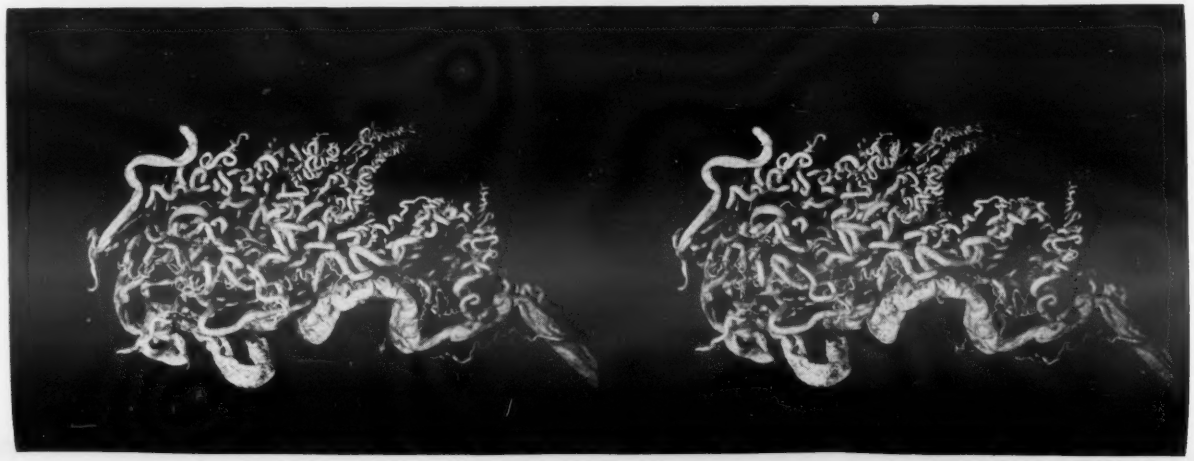


Fig. 6.—Injection-corrosion preparation of the arterial pattern in a 47-year-old multiparous woman six years past the menopause with history of chronic alcoholism and carcinoma of intestine. Blood pressure 160/90. Postmortem specimen. Uterine arteries injected. Compare with Fig. 1, since both are casts from postmenopausal women, and both suggest vascular inactivity. Arterial branches are sparse, thin, widely separated, small, and very slightly spiralled. See Table I, A, no. 28 (×2).

Fig. 7.—Injection-corrosion preparations of the arterial and venous patterns in a 43-year-old woman who was para ii, gravida i, with history of menometrorrhagia, and fibroid uterus. Blood pressure 170/100. Surgical specimen. Hysterectomy and bilateral salpingo-oophorectomy. Uterine artery injected. See Table I, C, no. 30, Observe the profuse arterial branching. In the upper right portion of the cast indicated by the arrow, there is a cast of a locally injected corpus luteum. The right half of this cast shows venous drainage of the corpus luteum. Compare with Figs. 1 and 6. Note also the difference in the distribution of the veins and arteries. Stereoscopic view (×1½).

Fig. 8.—Injection-corrosicn preparation of the arteries from a 42-year-old multiparous woman with cirrhosis of liver having menometrorrhagia. Blood pressure 120/80. Postmortem specimen. See Table I. D, no. 18. This patient had grossly sclerotic ovaries, yet showed numerous arterial branches. Grossly sclerotic ovaries do not, therefore, necessarily mean inactive ovaries. Compare with Figs. 1 and 6. These latter also had sclerotic ovaries. Stereoscopic view (×2).



menopause; and (4) gross appearance of sclerotic ovaries. By grossly sclerotic ovaries is meant a condition in which the ovaries are small, white, hard, and rugose. They have a gross appearance which is indicative of inactive, or senile organs. Table I, A, nos. 12, 28, 32, 37, demonstrate in a comparative form all pertinent history with respect to these cases.

Fig. 9.—Injection-corrosion preparation of the ovarian artery from a seven-month premature infant that died shortly after birth. Injection by way of the lower aorta. Cast shows some slight spiralling of the tertiary arteries. Arrow points to ovarian area. See Table II. Stereoscopic view (×5).

TABLE I. PERTINENT CLINICAL DATA RELATIVE TO PATIENTS FROM WHOM ARTERIAL PATTERNS WERE OBTAINED

NO.	AGE	BLOOD PRESSURE	L.M.P.	GROSS OVARIES	ENDOMETRIUM
A. *Subjects hypertensive and postmenopausal*					
12	53	210/112	1943	Sclerotic	
28	47	160/ 90	1941	Sclerotic	
32	73	212/ 55	Many years	Sclerotic	
37	51	160/ 96	1940	Sclerotic	Atrophic
B. *Subject nonhypertensive; recent menopause*					
23	54	136/ 60	1945	Sclerotic	Proliferative
C. *Subjects hypertensive and premenopausal*					
16	42	170/100	Sept. 1947	Cystic	
30	43	170/100	Menometrorrhagia	Cystic	Early secretory
D. *Subjects nonhypertensive and premenopausal*					
18	42	120/ 80	Menometrorrhagia	Sclerotic	
39, 40*	46	140/ 80	Sept. 23, 1947	Sclerotic	Proliferative
41	47	150/ 65	Oct. 20, 1947	Sclerotic	Early secretory

*Nos. 39 and 40 were specimens from same patient.

Ovaries from another patient (no. 23, Table I, B) with a similar type of history and clinical findings as the foregoing ones were also studied. This patient differed, however, in that she was nonhypertensive, and her menopause was more recent. The endometrium still showed proliferative changes. The cast of her ovarian arteries, shown in Fig. 2, shows branches that are definitely smaller, thinner, and more widely spaced than those seen in more active ovaries (Figs. 7 and 8).

Ovaries were obtained from two other patients with hypertension (Table I, C, nos. 16 and 30) but not past the menopause. Their ovaries were not grossly sclerotic. These patients were below the fifth decade in age. The arterial casts from these ovaries reveal a relatively luxuriant and profuse appearance of the arterial branches (see Fig. 7).

Three patients are presented who were nonhypertensive and nonmenopausal (Table I, D, nos. 18, 39, 40, 41). Their ovaries were grossly sclerotic. These, too, showed an active or more profuse growth of arterial branches (see Fig. 8).

Although these data are few, they suggest that sparse, small, thin, and widely spaced arterial branching of the primary, secondary, and tertiary ovarian arteries (Figs. 1 and 6) are related to the menopause. This conclusion suggests that to the known trophic activities of estrogens we may now add also that of growth and development of the primary, secondary, and tertiary branches of the ovarian artery. Case number 23 in Table I, B and Fig. 2 suggests an ovarian vascular system that has not reached the end point of vascular involution represented by Figs. 1 and 6. The degree of involution is not complete. It may be that this patient had some extraovarian source of estrogenic stimulation. In fact, hyperplasia of the endometrium has been found in patients with long-standing menopause long after proved cessation of ovarian activity. It has been suggested that the adrenal cortex may have an estrogenic function after the ovary ceases its activity.[13] The gross appearance of small sclerotic ovaries does not necessarily, therefore, portray quiescent vascular structures within the ovary.

Fetal and Neonatal Ovary.—The arterial cast from the ovary of a seven-month premature infant is shown in Fig. 9. In this, a slight degree of spiralling can be observed. In addition, preparations have been made from five other full-term and infant ovaries. The data are most interesting when tabulated in a chronological fashion, as in Table II.

TABLE II. CONFIGURATIONS OF OVARIAN ARTERIES IN PREMATURE AND INFANT OVARIES

NO.	AGE	GROSS OVARIES	ARTERIAL CONFIGURATION
31	Premature—7 month	Normal	Slight spiralling
44	Full term—stillborn	Normal	Slight spiralling
36	Full term—7 hr.	Normal	Slight spiralling
47	Full term—9 days	Normal	Excellent spiralling and more profuse branching
43	Full term—3 mo.	Two small atretic follicular cysts—left ovary	No spiralling
59	Full term—4½ mo.	Polycystic	Some spiralling with evidence of "paying-out" and many straightened arterial branches

From the seventh month of gestation until a short time after birth, growth and development of this vascular pattern in all specimens may be noted. This ranges from a slight degree of spiralling to excellent spiralling of the primary, secondary, and tertiary ovarian arteries. At three months of age, however, there is no trace of spiralling. At four and one-half months, some extended spirals may be seen and there are many straightened arteries in all branches.

The presence of cysts in infant ovaries and their relationship to arterial spiralling will be presented more fully in a future publication. It would seem, however, that the presence of spiralling, and its regression in fetal and infant ovaries, is dependent on a maternal hormonal influence. Maternal hormones have been recognized in the past as being an influential factor in newborn breast enlargement, lactation, endometrial bleeding and vaginal hypertrophy. In the latter case, desquamation begins in forty-eight to sixty hours post partum and

complete, infantile atrophy appears at the end of the first three weeks of postnatal life. Seventy-five per cent of infants will lactate until three to four months of age.[10]

Scammon,[11] investigating the subject of uterine growth, observed that the fetal uterus grows uniformly until the seventh month of intrauterine life. After this period, an acceleration in the rate of uterine growth occurs. He suggested that "growth of the uterus in the latter fetal months consists of a substrate of typical fetal growth plus a secondary growth increment, which presumably is due to an extra stimulus furnished by a hormone of placental or possibly ovarian origin. After birth, the organ loses this secondary increment but retains that resulting from the early fetal growth rate." Within a few days after birth, the uterus diminishes in size. However, a fortnight after birth the uterus is the size of that noted in 11-year-old females.[12]

From the evidence presented in Table II, and keeping the above discussion in mind, it is suggested that maternal hormones may stimulate the development of spiralling and branching of the primary, secondary and tertiary arteries in the ovary beginning late in fetal life. The action is most marked about one week after birth. Regression takes place over a period of several months after the maternal influence is withdrawn by parturition.

Ovarian Veins.—The casts of ovarian veins are quite different morphologically from those obtained from the arterial system and can be easily identified. We have confirmed Farre that the veins of the ovary drain into a pampiniform plexis[4] in the hilar area. They are large, irregularly tortuous, markedly flattened, and often appear matted (compare Figs. 4, 5). The various branches anastomose with each other very frequently. This contrasts with the ovarian arteries which show no evidence of vascular anastomoses. Within the substance of the ovary, the veins end in small, straight channels that are never spiralled. Occasionally small, pouch-like protuberances were noted in larger branches in the vicinity of the hilus. Sometimes a beading may be noted in the medium veins that may be mistaken for spiralling on superficial examination.

Summary

A study of vascular patterns in the human ovary has been presented.

The vascular system in the human ovary is more complex than that of the rabbit. However, it shows helical spiralling with gradual diminishing diameters in the branches of the main ovarian artery. The function of spiralling in the ovarian branches of the arterial system are (1) adaptation of the vasculature to ovarian growth, and (2) to provide a mechanism for the reduction and regulation within the ovary of blood pressure.

A relationship exists between arterial spiral distortion resulting from ovarian cysts, corpora lutea, and the arrangement of the ovarian veins.

Characteristics of the ovarian artery and its branches have been described.

The relation of the condition of the vessels to ovarian activity and inactivity have been discussed.

It is suggested that there is a relation between growth and development of ovarian arterial branches and estrogenic activity in the adult.

Evidence is presented to show that branching of the arteries in the ovary from late fetal life to shortly after birth is under the influence of maternal hormones.

Observation of the venous vascular tree shows completely different characteristics when compared to the arteries.

Acknowledgment is hereby made to Dr. Silik H. Polayes for his kind assistance in making specimens and facilities available for this study. We are also indebted to Mr. Chester F. Reather, photographer in the Department of Embryology, Carnegie Institution of Washington, for his excellent photographs of the injection-corrosion casts of the ovarian blood vessels.

References

1. Reynolds, S. R. M.: Am. J. Obst. & Gynec. **53**: 221, 1947.
2. Hunter, William: Anatomia uteri gravidi tabulis illustrata, 1774.
3. Daron, G. H.: Am. J. Anat. **58**: 349, 1936.
4. Farre, Arthur: The Uterus and Its Appendages; the Cyclopedia of Anatomy and Physiology, ed. Robert B. Todd, Longman, Brown, Green, Longmans and Roberts, London, 1858.
5. Belou, P.: Revision Anatomica del Sistema Arterial, III. Atlas Estereoscopica de Anatomia de las Arterias; Segunda parte, p. 114 (Estereos 215), Buenos Aires, 1934.
6. Reynolds, S. R. M.: Endocrinology **40**: 381, 1947.
7. Reynolds, S. R. M.: Endocrinology **40**: 388, 1947.
8. Reynolds, S. R. M.: Acta anat. in press, 1948.
9. Delson, B., Lubin, S., and Reynolds, S. R. M.: Endocrinology, in press, 1948.
10. Smith, C. A.: The Physiology of the Newborn Infant, Springfield, Ill., 1945, Charles C Thomas, pp. 260-263.
11. Scammon, R. E.: Proc. Soc. Exper. Biol. & Med. **23**: 687, 1926.
12. Scammon, R. E.: The growth of the human reproductive system. Proc. Second. Intern. Cong. Sex. Res., p. 118.
13. Novak, E.: Gynecological and Obstetrical Pathology, Philadelphia, 1940, W. B. Saunders Company, pp. 139-141.

Discussion

DR. S. R. M. REYNOLDS.—The essential features of Dr. Delson's work are twofold. He has, first, analyzed the normal vascular patterns of the human ovary and shown the homology of parts between these and the simpler structures found in the rabbit ovary. Second, he has shown that the coils of the ovarian spiral arteries depend upon estrogens for their growth, development and maintenance. This is clearly a factor of some consequence to the gynecologist who must understand how to deal with the problem of primary amenorrhea, if there are no other signs of hypopituitarism. I think that Dr. Delson did not emphasize the point sufficiently that the evidence is clear that in those instances in which no estrogen has been produced, long after the menopause, there are few or no spiral vessels. The condition is not related to either hypopituitarism or sclerosis. This is highly significant, and it may well have an important meaning in the cases of amenorrheic females 18 or 19 years of age with no evidence of anterior pituitary gonadotrophic secretion. It may mean that estrogen is needed as a stimulus for the blood vessels of the ovary. And if this premise is correct, maturity is in part the result of the gonadotrophic hormone acting through the ovarian cortex, stimulating growth, and building up an adequate ovarian vasculature over the years until there is full maturity of the ovary.

It is of interest to the morphologist that estrogens have this particular trophic action upon the coiled vessels of the ovary. They have an exactly similar action upon the coiled arterioles of the uterus. Okkels and Engle observed ten years ago that with complete estrogen deprivation only part of the uterine spiral arterioles degenerate, namely, the spiral arterioles of the endometrium. What there is in common, histologically speaking, between these vessels of the ovary and the uterus remains to be established.

Dr. Delson stated that one of the functions served by the ovarian spiral vessels is the lowering of the blood pressure within the ovary. That is a very handy method of controlling the local circulation because the ovaries are more or less closely attached to the uterus in its outer part, and when the uterus is pregnant the ovaries become displaced with the uterus. Isn't it a convenient mechanism that moves the regulator of local blood pressure with the

ovary as it moves? In the rabbit, I have measured blood pressure in the ovarian artery about a centimeter or two away from the ovary. The necessity for lowering of the blood pressure within the ovary is shown by the fact that the blood pressure in the ovarian artery is about 30 to 50 per cent that in the carotid artery. The necessity exists, therefore, for lowering rapidly the blood pressure in the ovary to near the level of the effective osmotic blood pressure in the plasma.

The effect of ovarian growth following gonadotrophic stimulation of the rabbit ovary shows that there is normally an even extension of the coiled artery. The effect is maximal at seventy-two hours after the injection of gonadotrophins, and over the next six days (as many stimulated Graafian follicles become atretic) the coil recovers.

In the rabbit the pattern is simple. However, Dr. Delson has seen that the same thing is occurring in the human ovary many times over since there are many more vessels. If we did not have the rabbit ovary as a basis of primary information, I doubt that we could understand the situation in the human, since the vasculature is so complex.

If cysts result from the injection of gonadotrophins, there is extreme distortion of the spiral arteries. The cysts are in the vicinity or, just distal to, the area of distortion.

The physiologic story that has been elaborated is opening up a new field of understanding of the relationship between the arteries and the flow of blood. In other words, if the latter is abnormal when follicles are growing rapidly cysts develop; if it is not abnormal they do not. There is reason to believe that hormonal stimulation produces generalized follicular growth; this normally gives rise to even extension of the spiral arteries. If the amount of follicular growth is excessive in some region of the ovary, then distortion of the spiral artery results, and with disorientation of the local hemodynamic relations, extreme swelling of the growing follicle ensues. I believe that this work of Dr. Delson's may open up a new chapter for the pathologist who is interested in interpreting the various kinds of ovarian pathology that he sees in the ovaries.

Dr. Delson's work shows, I believe, that these simple lesions which are so easily seen in the rabbit occur in the human being as well. However, instead of a single coiled vessel, there are numerous coiled vessels, and these offer multiple chances for localized ovarian dysfunction. The gynecologic pathologists will, I believe, tell us much concerning this unwritten chapter of gynecology.

A SURVEY OF FUNCTIONAL UTERINE BLEEDING WITH SPECIAL REFERENCE TO PROGESTEROGEN THERAPY

G. E. Seegar Jones, M.D., and R. W. Te Linde, M.D., Baltimore, Md.

(From the Department of Gynecology, Johns Hopkins Hospital and University)

FUNCTIONAL uterine bleeding is a major problem in gynecology, as it frequently occurs in young individuals and causes such severe symptoms that treatment is imperative. Yet, by definition, the uterus is normal. Under these conditions, radical therapy such as hysterectomy or irradiation for the control of bleeding is to be avoided if possible.

It has long been recognized that the endometrial pattern of functional uterine bleeding is not uniform. Consequently, the response to therapy might also vary, depending upon the associated endometrial pattern.

With this in mind, an effort has been made to analyze cases of functional uterine bleeding seen in the gynecologic out-patient department at the Johns Hopkins Hospital, to determine the relationship between the endometrial pattern and the response to therapy.

Method of Case-Handling

Patients having functional uterine bleeding were subjected to an initial curettage. This procedure served the dual purpose of establishing the diagnosis and instituting the simplest form of therapy. There has been a satisfactory response in approximately 42 per cent of all cases treated in this clinic by a single curettage.[1] Only if abnormal bleeding recurred, was a case referred to the functional bleeding clinic for special consideration.

In 1942, the authors reported the results of progesterogen therapy in cases of functional uterine bleeding associated with endometrial hyperplasia.[1] The present study extends to all types of endometrial patterns, but the method of therapy has remained essentially unchanged. An initial dose of 30 mg. of pregneninolone* a day was given orally for seven days. Therapy usually followed a suction curettage, as all patients were bleeding abnormally when treatment was begun. The Novak suction curette is preferred because, although it requires a slightly more complicated apparatus, it is more versatile in its use. With the continuous type of suction, rather than a plunger type, a discrete biopsy can be obtained or a fairly thorough curettement performed if desired. The initiation of therapy could not be related to any specific time of the cycle as the patients were not having cyclic bleeding. Twenty-eight days after the first progesterogen therapy, the second course of seven days of medication was begun, using the same dosage. The third therapeutic cycle was given for from five to seven days beginning twenty-one days after the onset of bleeding following the second course of progesterogen therapy. If, during the second and third months of therapy, the therapeutic response was satisfactory, that is, if the bleeding began within five days of cessation of therapy and lasted no longer than seven days, medication was discontinued. The patients were carefully watched during the next few months, and if excessive or prolonged bleeding recurred, therapy was resumed.

*Progestoral (Roche-Organon, Inc., Nutley, N. J.)

While the bleeding symptoms were being controlled by hormonal therapy, attempts were made to evaluate the etiological factors underlying the condition. Routine laboratory studies consisted of a basal metabolic rate, blood cholesterol, fasting blood sugar, and a complete histologic blood study. Medical consultations were routinely requested, as were psychiatric consultations when indicated. Additional laboratory data, consisting of glucose tolerance tests, urinary 17-ketosteroid determinations, x-rays of the sella turcica and chest, as well as examinations of the visual fields were obtained only when indicated. Following the first two months of cyclic progesterone, some form of adjunctive therapy, consisting of diet or thyroid, was begun as indicated.

Material

A total of 104 cases were studied in the functional bleeding clinic during the past seven years. The records of 212 patients with functional bleeding seen in the gynecologic out-patient department during the years 1940 and 1945 were reviewed for comparisons. It is significant that only 36 cases, or 17 per cent of the above 212 cases, were considered suitable for study in the special functional bleeding clinic (Table I). This means that such patients had repeated attacks of prolonged or profuse bleeding not checked by curettage and were in the younger age group. That age has played a major role in determining which cases should be referred for consideration of conservative therapy is shown in Table II.

TABLE I. ENDOMETRIAL FINDINGS IN CASES OF FUNCTIONAL UTERINE BLEEDING

ENDOMETRIAL PATTERN	STATISTICS FOR OUT-PATIENT DEPARTMENT			STATISTICS FOR SPECIAL FUNCTIONAL BLEEDING CLINIC, YEARS 1940-1947	
	1940	1945	TOTAL PER CENT	PER CENT	ORIGINAL DIAGNOSIS
Hyperplasia	30 (16)*	25 (14)	26	66	69
Interval nonsecretory	26 (1)	21 (4)	22	16	17
Endometritis chronic	34 (1)	13	22		3
Postmenstrual	5	5			0
Atrophic	1	–			2
Menstruating	1	4			–
Secretory	24	23	22	12 (4)†	13 (4)†
Total	212 (36)				104

*Indicates the total number of cases referred to the Special Functional Bleeding Clinic.
†Indicates the total number of true functional cases. See Table VII.

TABLE II. AGE DISTRIBUTION OF CASES SHOWING FUNCTIONAL BLEEDING WITH NONSECRETORY ENDOMETRIUM

AGE IN YEARS	OUT-PATIENT DEPARTMENT CASES YEARS 1940 AND 1945		SPECIAL CLINIC CASES 1940-47	
	CASES	PER CENT	CASES	PER CENT
11 to 20	13	12	25	27
21 to 30	37	35	46	51
31 to 40	30	29	11	12
Over 40	25	24	9	10
Total	105	100	91	100

Endometrial Patterns

The types of endometrial patterns found in the groups of patients studied can be seen in Table I. The statistics from the special clinic agree quite well

with those reported by Jones in 1938,[2] but the out-patient department statistics vary somewhat. This variation probably reflects the fact that the criteria for the diagnosis of chronic endometritis during the year 1940 were apparently more liberal than in other years.

In both the out-patient department and the special clinic, endometrial hyperplasia comprised the largest group of cases on the basis of the original curettage, this being 69 cases, or 66 per cent of the special clinic group. To substantiate further the feeling that severe functional bleeding is most commonly associated with the pattern of endometrial hyperplasia, it is noted that, during the years 1940 and 1945, 54 per cent of the patients with endometrial hyperplasia seen in the general dispensary were referred to the special clinic, while only 10 per cent of those showing interval non-secretory endometrium and no appreciable percentage of the other endometrial types was referred.

The majority of patients in the special clinic group had been curetted for recurrences on numerous occasions. The results of study of the total 234 curettages performed on the 104 patients have been tabulated in Table III. In approximately 37 per cent of cases, the histologic picture changed in successive curettings from the same patient. The main variation, however, was between hyperplasia and interval nonsecretory endometrium (Table IV). It is significant that, in the present series at least, hyperplastic or nonsecretory endometrium never varied with a secretory pattern while the patients were having symptoms. Curettings taken to evaluate therapy when patients were asymptomatic have not been included. Many were secretory immediately after progesterogen therapy (Fig. 1). Only two curettements were made on patients who were having regular menses from six to eight months after therapy. Both showed secretory endometrium (Fig. 2).

The variations of pattern found in the secretory group corresponded to the menstrual dates except in the one instance of chronic endometritis. This curettage was done on a patient with thrombocytopenic purpura who had been bleeding profusely nine days.

Results of Therapy According to Endometrial Patterns

Endometrial Hyperplasia.—Sixty-nine of the 104 special clinic patients showed endometrial hyperplasia at the initial curettage. Forty-four, or 64 per cent, showed an unchanging hyperplastic pattern on every subsequent curettage, while 25, or 36 per cent, showed some variation (Table III). By far the most common histologic variation was between hyperplastic and interval nonsecretory endometrium. Several patients showed three different types of endometrial patterns on successive curettements during the seven-year period (Table IV).

TABLE III. CHANGE IN ENDOMETRIAL PATTERNS FOUND IN A STUDY OF 234 REPEATED CURETTAGES ON 104 SPECIAL CLINIC PATIENTS

ENDOMETRIAL PATTERN	NO. OF CASES FOUND AT ORIGINAL CURETTAGE	NO. OF CASES SHOWING NO CHANGE IN PATTERN	NO. OF CASES SHOWING CHANGE IN PATTERN
Hyperplasia	69	44 (64%)	25 (36%)
Interval nonsecretory	17	12	5
Endometritis chronic	3	1	2
Postmenstrual	0	–	–
Atrophic	2	2	0
Menstruating	0	1	–
Secretory	13	6	7
Total	104	65 (63%)	39 (37%)

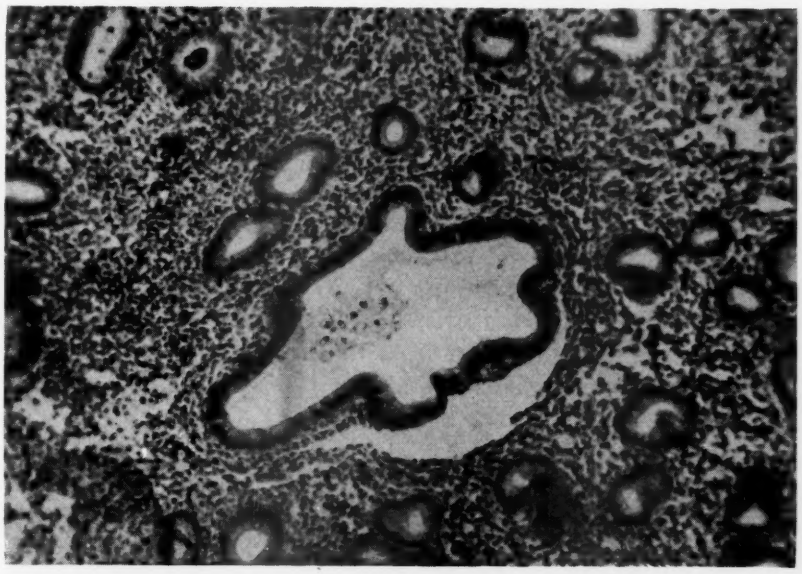


Fig. 1, *A*.—Curettings obtained immediately before therapy. Photomicrograph. Low power.

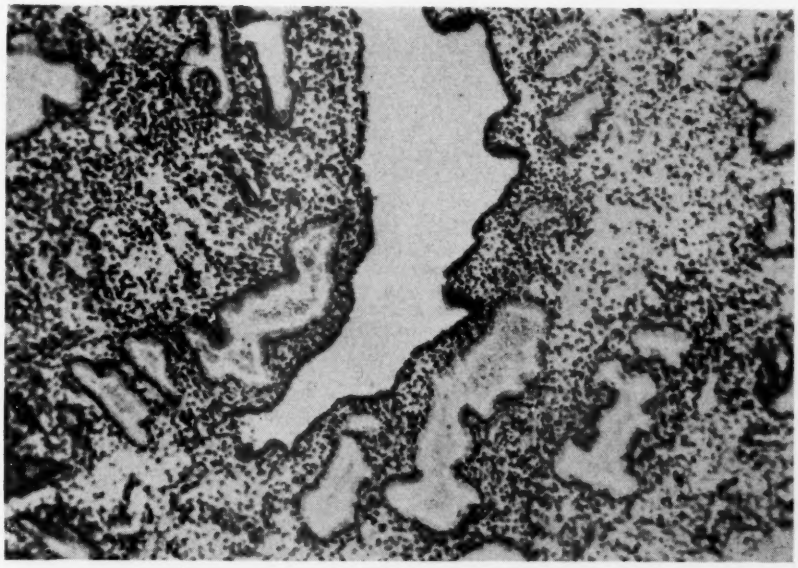


Fig. 1, *B*.—Curettings from the same patient after a total of 402 mg. of pregneninolone over a period of seven days. This dosage is necessary to produce a secretory pattern but half the amount will control the bleeding symptoms. Photomicrograph. Low power.

TABLE IV. VARIATIONS IN PATTERNS WHICH OCCURRED WITH RECURRENCE OF SYMPTOMS AS SHOWN IN 130 SUBSEQUENT CURETTINGS FROM 104 CASES OF FUNCTIONAL BLEEDING

ENDOMETRIAL PATTERN AT ORIGINAL CURETTAGE	NO. OF SUBSEQUENT CURETTAGES SHOWING THE FOLLOWING PATTERNS					
	HYPERPLASIA	INTERVAL NONSECRETORY	ENDOMETRITIS CHRONIC	POSTMENSTRUAL	MENSTRUAL	SECRETORY
Hyperplasia (69)	71	27	4	0	0	0
Interval nonsecretory (17)	10	9	3	1	0	0
Endometritis chronic (3)	1	1	0	0	0	0
Atrophic (2)	0	0	0	0	0	0
Secretory (13)	0	5	1*	1	1	0

*Obtained after a profuse nine-day menstrual period in a patient with thrombocytopenic purpura.

Fifty-six of the sixty-nine cases were considered suitable for progesterogen therapy and in this group there were no therapeutic failures (Table V). The establishment of regular menses while on therapy was the criteria of success. Two patients had subsequent x-ray castration because of recurrences. These women were both parous and in the older age group, one being 42 years old at the time of x-ray therapy. One patient had a bilateral salpingectomy and hysterectomy subsequently because of pelvic inflammatory disease.

TABLE V. RESPONSE TO PROGESTEROGEN THERAPY IN 74 CASES OF FUNCTIONAL UTERINE BLEEDING SHOWING NONSECRETORY ENDOMETRIUM

ENDOMETRIAL PATTERN	CASES TREATED	SATISFACTORY RESPONSE	UNSATISFACTORY RESPONSE	RECURRENCE OF SYMPTOMS	NO RECURRENCE
Hyperplasia	56	56	0*	31 (55%)	25 (45%)
Interval nonsecretory	15	13	2†	7	6
Endometritis chronic	1	1	0	1	–
Atrophic	2	2	0‡	1	1
Total nonsecretory treated	74	72	2	40	31

*Two subsequent x-ray castrations in older parous women with recurrences. One subsequent hysterectomy, bilateral salpingectomy because of inflammatory disease.

†One patient had an ovarian neoplasm and the other a concomitant pelvic inflammatory disease which was controlled by chemotherapy.

‡One patient treated for recurrence elsewhere by intrauterine radium.

There were five atypical responses. Cases were considered atypical in response to therapy if the patient did not stop bleeding within eight days after cessation of the first progesterogen therapy; if bleeding recurred before 28 days after beginning of the first progesterogen course; or if bleeding lasted over six days following any subsequent course of progesterogen.

Of the fifty-six successfully treated cases, 25, or 45 per cent, had no recurrence of symptoms after the first three-month course of progesterogen therapy. If these 25 cases are analyzed as to adjunctive therapy, we find that 13, or about 50 per cent, had no other therapy. This might suggest that progesterone itself effects a cure. Thyroid medication was indicated and used, apparently successfully, in six patients with basal metabolic rates below –5 per cent or blood cholesterol values above 250 mg. per cent; an additional two patients were treated with desiccated thyroid and high protein, low caloric diets; three patients were treated by diet alone.

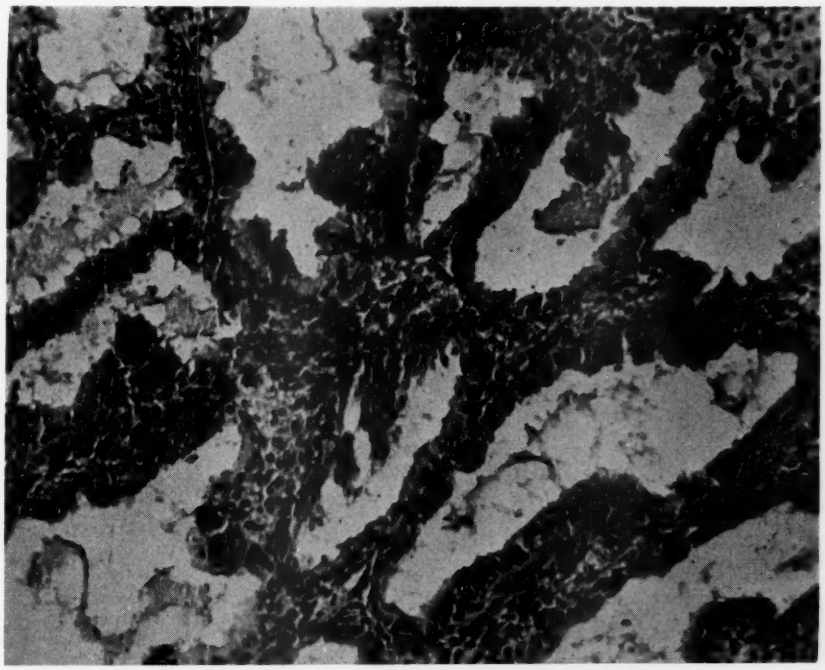


Fig. 2.—Curettings from a patient during a period of remission taken six months after the last therapy. Patient had been having regular menses. Photomicrograph. Low power.

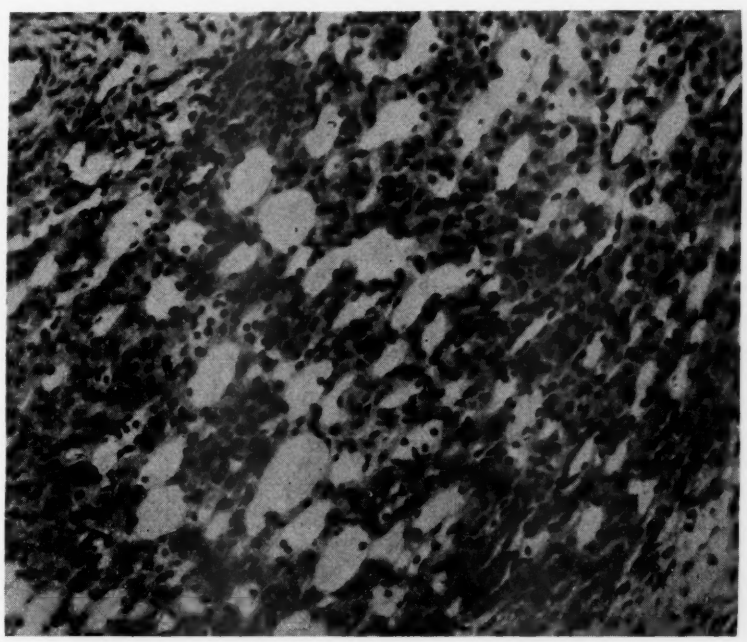


Fig. 3.—Tissue found in the hilum of the ovary of patient having functional bleeding which was irresponsive to progesterogenic therapy. Photomicrograph. Low power.

Thirteen cases were not treated with progesterone. Of these, five were treated successfully by high protein, low caloric diets with supplementary vitamins; two responded to thyroid, 0.1 Gm. (1½ grains) a day; two, with bleeding associated with pelvic inflammatory disease, were treated with douches and chemotherapy. Three patients in the menopausal group and an additional one with hypertension were advised to have irradiation therapy.

Forty-eight of the fifty-six women were married and ten of them subsequently became pregnant (Table VI).

TABLE VI. OBSTETRICAL HISTORIES BEFORE AND AFTER PROGESTERONE THERAPY OF PATIENTS WITH NONSECRETORY ENDOMETRIUM

ENDOMETRIAL PATTERN	CASES TREATED	MARRIED	PREGNANCIES BEFORE TREATMENT	PREGNANCIES AFTER TREATMENT
Hyperplasia	56	48	32	10
Interval nonsecretory	15	12	5	1
Endometritis chronic	1	0	0	0
Atrophic	2	1	0	0
Total	74	61	37 60%*	11 18%*

*Of married women.

The following case report is presented in detail because it seems to represent perhaps the most serious problem in a consideration of functional uterine bleeding: *the differentiation of benign endometrial hyperplasia and adenoma malignum.* It may serve as a warning that patients with very small malignancies of the fundus may respond to cyclic progesterogen therapy if the major portion of the bleeding is due to an associated endometrial hyperplasia. It is, therefore, extremely necessary to have thorough curettages in all cases before therapy is begun. In addition, endometrial biopsies should be obtained before patients with recurrent symptoms are treated, if a period of a year or more has elapsed since the original curettage.

Mrs. E. G., a 54-year-old white woman, para 3-0-0-3, had been bleeding profusely and almost constantly for about two years. A curettage had been performed elsewhere the previous year with only very temporary relief of symptoms. The diagnosis at that time was reported to be endometrial hyperplasia. The patient was curetted and advised to have a hysterectomy because of the pseudomalignant pattern of the endometrium (Fig. 4, *A*). She refused operation, and was not free of symptoms following her curettage so was placed on cyclic progesterogen therapy, 30 mg. a day of pregneninolone for seven days, as a palliative measure while she considered further treatment. Her response was satisfactory and the following month she again received cyclic progesterogen therapy. An endometrial biopsy was taken after treatment the second month and marked squamous metaplasia was found (Fig. 4, *B*). Hysterectomy was again advised and this time the recommendation was accepted. At operation, the uterine lining appeared to be compatible grossly with benign polypoid hyperplasia but, on microscopic examination, a small area of hyperactivity was seen in the region of the right cornu (Fig. 4, *C*) which under higher power was diagnosed as adenoma malignum (Fig. 4, *D*). There was no invasion of the myometrium and the patient is living and well three years postoperatively.

Interval Nonsecretory Endometrium.—Seventeen cases, or 16 per cent, showed interval nonsecretory endometrium on the initial curettage. Subsequent curettings on five of these women showed hyperplasia or chronic endometritis (Table IV).

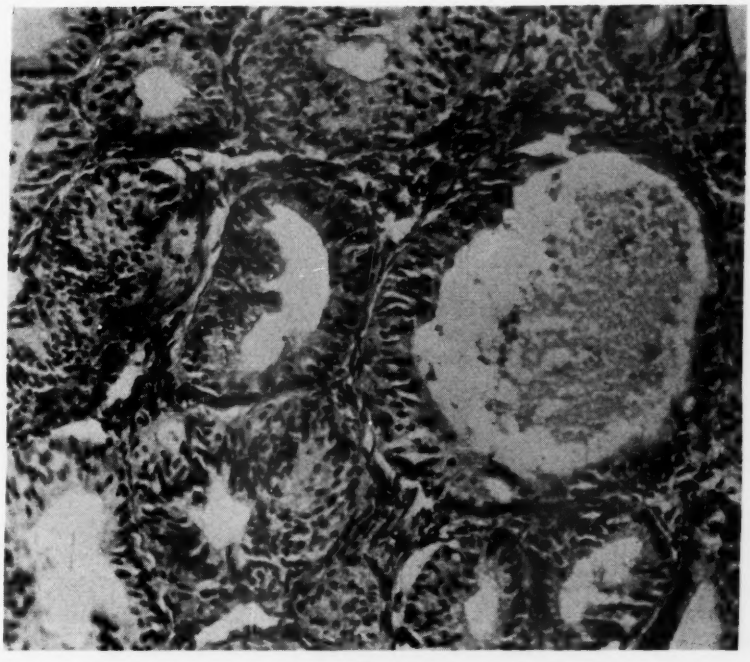


Fig. 4, *A*.—Curettings from E. G. obtained before therapy. There are areas suggestive of metaplasia and a marked decrease in the stromatogenous elements. Photomicrograph. Low power.

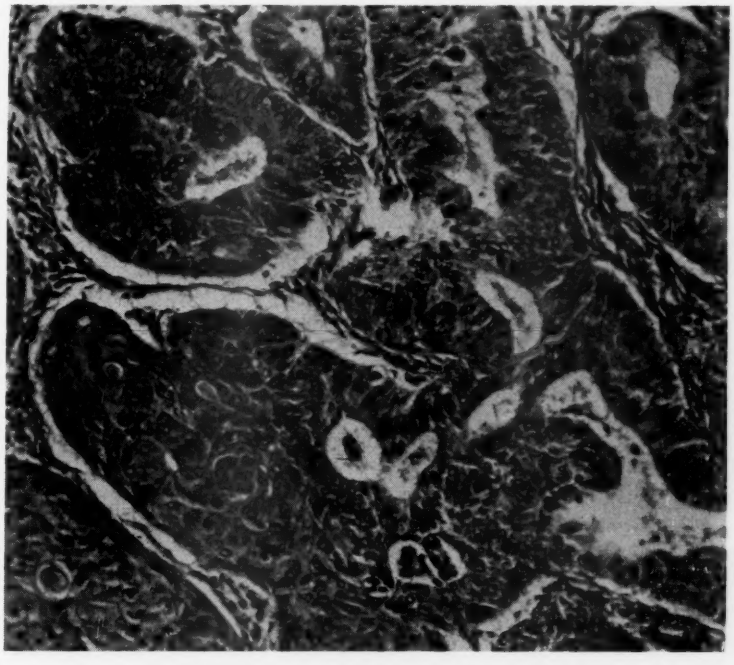


Fig. 4, *B*.—Curettings obtained after second month of cyclic progesterogenic therapy. There is marked squamous metaplasia. Photomicrograph. High power.

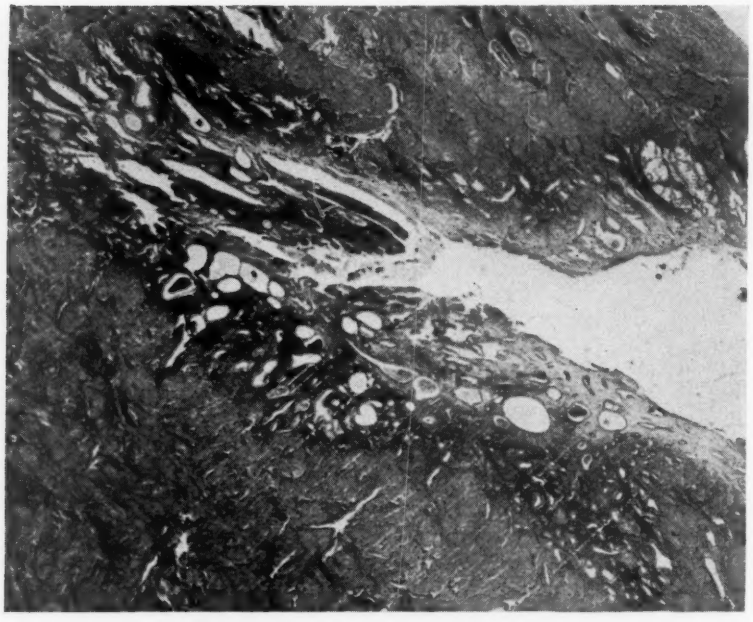


Fig. 4, *C.*—Endometrial lining obtained at hysterectomy. There is a small, extremely cellular adenomatous area in the upper right corner. Photomicrograph. Low power.

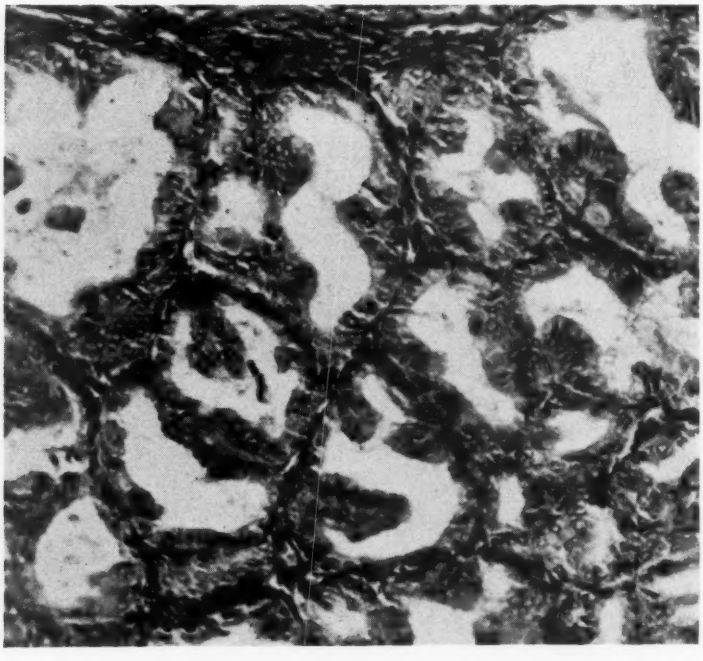


Fig. 4, *D.*—A high power photomicrograph of the adenomatous area showing adenomalignum.

Fifteen patients were judged suitable for progesterogen therapy. Thirteen had excellent results. Five of these have had no recurrence following discontinuation of cyclic progesterone. Of these five, three had no adjunctive treatment, and two had necessary dietary adjustments.

Two patients failed to respond to progesterogen therapy. One was a 24-year-old Negro woman who was thought to have typical functional bleeding but continued to have a bloody discharge throughout treatment. Pelvic inflammatory disease was suspected and the bleeding yielded to chemotherapy and douches. The second failure was in a 19-year-old obese patient who had a diagnosis of chronic endometritis on her second curettage. Because of a palpable enlargement of the right ovary, a laparotomy was performed and an enlarged ovary resected. Grossly no tumor was detected, but microscopically there was a diffuse collection of chromaffin-like cells in the hilum (Fig. 3). The patient has remained well following this operation and is now pregnant two years later.

Two patients were not treated with progesterone. Both were young girls, 12 and 16 years of age, in the first year of their menstrual life. Both responded to general hygienic measures consisting of improvement in eating, sleeping, and work habits.

The histories, symptoms, and clinical findings in this group of patients were identical with those found in the group with the diagnosis of endometrial hyperplasia.

Chronic Endometritis.—Three patients showed chronic endometritis when first curetted. Two had variations in patterns on subsequent curettages (Table IV). Only one patient received hormone therapy. This 22-year-old Negro woman had had irregular, excessive vaginal bleeding since her menarche, 9 years before. She received two courses of progesterogen therapy, and had a recurrence of symptoms six months after cessation of her primary therapy. Two years later she was asymptomatic, except for some irregularity in her menstrual interval. The second case was seen following her second curettage but did not return for therapy. The third patient had hypertension and was advised to have x-ray castration. She refused and was unimproved symptomatically when last seen five months after curettage.

Atrophic Endometrium.—Two cases of atrophic endometrium were studied. Both were young women, 19 and 21 years of age, who had had numerous curettages elsewhere. One had received a small dose of intrauterine radium. Bleeding was exsanguinating, in both cases necessitating repeated transfusions. Pregneninolone had been used in both cases elsewhere and was reputed to have been unsuccessful. Both were treated successfully by giving from 1 up to 3 mg. of stilbestrol a day for seventeen days, followed by a seven-day course of from 5 to 10 mg. of progesterone intramuscularly. Of these, the first patient had to leave the city, and had a recurrence of symptoms almost immediately after cessation of therapy. Intrauterine irradiation was used at that time. The second patient has been treated for five months, and is still having therapy. It will be noted that these cases were extremely severe, and that they did not receive a trial of oral progesterone in our clinic because of the story of failure elsewhere. It is, therefore, not definitely known how such patients would respond to oral medication for histories as given by patients are notoriously unreliable. It is also impossible to evaluate the use of estrogens in these cases because there is no control period. However, it seems that if estrogen were ever indicated, it would be in cases showing little or no endometrium.

Secretory Endometrium.—Among those referred to the special clinic, there were thirteen patients who initially, or without therapy, showed secretory endometrium. There was a striking difference in the symptomatology of these patients, as the complaint was prolonged or profuse menses with intermenstrual spotting in nine cases, while only four of the thirteen women had any irregularity of the menstrual interval. After a period of study, a number of these patients were eventually shown not to have true or uncomplicated cases of functional uterine bleeding (Table VII). One had had profuse, prolonged menses over a period of four years and, finally, at hysterectomy, proved to have a submucous myoma and adenomyosis. Another developed palpable endometriosis while under observation. Two had associated pelvic inflammatory disease and acute cervicitis with positive Neisserian cultures, while an additional two had parametritis following abortions. All four patients with inflammatory processes were successfully treated by chemotherapy, douches, and bed rest. One of these is now pregnant after a two-year history of profuse bleeding and sterility.

Seven patients had functional bleeding in the light of the original definition, e.g., there was no abnormality in the uterus; however, two of these had thrombocytopenic purpura and one had hypertension. The remaining four seemed to have functional disturbances representing abnormalities of the corpus luteum function. These latter patients had a disturbance of the menstrual interval represented by prolonged, irregular cycles followed by profuse, prolonged menses. Two were women who had exhibited such disturbances throughout their menstrual lives, and probably had true endocrine dyscrasias. The other two had a sudden onset of symptoms correlated with acute psychiatric disturbances. All four women had small ovarian cysts at the time of curettage, and the first two patients had been temporarily relieved of symptoms elsewhere by operative removal of ovarian cysts. Although it is expected that these were probably corpus luteum cysts, unfortunately, no pathologic report is available to corroborate the diagnosis.

Six of the thirteen patients (Table VII) were treated unsuccessfully with progesterone. It was believed that such an unsuccessful result was to be expected, as surely there is no rationale for such therapy.

TABLE VII. FINAL DIAGNOSIS AND ANALYSIS OF CASES SHOWING SECRETORY ENDOMETRIUM SEEN IN THE SPECIAL FUNCTIONAL BLEEDING CLINIC

FINAL DIAGNOSIS	NO. CASES	DISTURBED MENSTRUAL INTERVAL	PROGESTERONE TREATED	SUCCESSFUL RESULTS
Thrombocytopenic purpura	2	0	1	0
Pelvic inflammatory disease and parametritis	4	0	2	0
Adenomyosis	1	0	1	0
Endometriosis	1	0	1	0
Hypertension	1	0	0	–
Corpus luteum cysts (?)	4	4	1	0
Totals	13	4	6	0

Discussion

From the present study, it was found that only about 17 per cent of the cases of functional uterine bleeding seen in the gynecologic out-patient department at the Johns Hopkins Hospital were severe enough or in the age group to require special treatment. The remaining 83 per cent were satisfactorily handled by simple curettage, or, if necessary, in the older age group, by hysterectomy or irradiation therapy.

It was further noted that of the 104 cases of functional bleeding referred during the past seven years for special consideration in the functional bleeding clinic, only seventy-one, or 69 per cent, were thought suitable for endocrine therapy.

A total of 234 curettages were performed on the same 104 patients. The initial diagnosis was hyperplasia in 66 per cent, interval nonsecretory in 16 per cent, secretory in 12 per cent, and other patterns (chronic endometritis, atrophic) in 6 per cent. Thirty-seven per cent of the cases showed no change in diagnosis on subsequent curettages. In the remaining 63 per cent, variations in patterns occurred. These were apparently mutually interchangeable among the nonsecretory groups. Patients with an initial diagnosis of secretory endometrium showed variations in pattern in subsequent curettements, but these were compatible with the day of the cycle at which the curettement was performed.

As the endometrial patterns were interchangeable among the nonsecretory groups, it might be assumed that the response to therapy would be uniform. This, indeed, seems to be the case, for if the patient with an ovarian neoplasm is excluded, there has not been a single failure of progesterogen therapy among the patients bleeding from a nonsecretory type of endometrium. The patients having an associated gonorrheal cervicitis should be excluded as unsuitable for treatment. The cases showing secretory endometrium, however, seem to have a different etiology and might be expected to respond differently to therapy. Not one case with secretory endometrial bleeding has been successfully treated by progesterone.

In the present series of cases, cyclic oral progesterogen therapy has been used almost entirely. In two cases having atrophic endometrium, from 3 to 5 mg. of stilbestrol were given daily for two weeks before beginning progesterogen therapy. These two patients and an additional three showing interval nonsecretory and hyperplastic endometrium seemed to respond better to intramuscular progesterone than to oral progeninolone. Therefore, in severe cases, especially in those with low hemoglobin, when it is important to control the symptoms as rapidly as possible, it is probably wiser to use the drug intramuscularly, at least in the first course of therapy. Thus, the variations in response to therapy which may be expected to occur with any oral medication can be avoided.

In using progesterogen therapy, two things should be emphasized; first, it is not a hemostatic drug, and bleeding does not cease until a week after progesterone withdrawal; second, it probably does not cure the underlying condition or conditions but only relieves the symptoms; therefore, recurrences are to be expected. In the present series, 57 per cent of the cases successfully treated had a return of symptoms within six months to two years after cessation of therapy. Recurrences have been successfully treated by another series of cyclic progesterogen therapy.

Although we have regarded progesterogen therapy as palliative only, it is interesting to note that about 50 per cent of the patients who had no recurrence of symptoms after the initial course of progesterone had no adjunctive therapy.

The fact that 18 per cent of all cases treated (Table VI) became pregnant is a strong argument for perseverence with conservative therapy of functional bleeding.

Because we do not believe that cyclic progesterogen therapy is a specific cure for functional bleeding, all patients are investigated to determine if possible what the etiological factors underlying the condition might be. Thirty-three women in the present series had indications of a lowered thyroid function as judged by a basal metabolic rate below –5 or blood cholesterol above 250 mg. per cent. Twenty-three of these women apparently responded to therapy; the usual dosage being 1½ to 2 grains a day over a period of at least four months. Thirteen of the twenty-three women were also on special reducing diets. Ten patients were unresponsive to thyroid and three were unsatisfactorily followed. Fifteen women were successfully treated by diet alone; one mild diabetic patient falls into this group. Two patients with mild hyperthyroidism were treated by bed rest and Lugol's solution. A number of patients who have been judged as successfully treated had recurrences because of lapses in therapy but in each case they have responded satisfactorily again to treatment.

In the present series it was found that true cases of functional bleeding from secretory endometrium are rare. Of the thirteen cases, only four, or approximately 4 per cent of the total series, were finally selected as being uncomplicated functional disorders. These four had ovarian cysts, which were probably corpus luteum cysts, and showed disturbances of the menstrual interval as did all of the nonsecretory cases. It is interesting that there were two cases of thrombocytopenic purpura in the group, which stresses the importance of keeping the medical aspects of the disease well in mind.

Summary

1. During the past seven years, approximately 700 cases of functional bleeding have been seen in the gynecologic out-patient department of the Johns Hopkins Hospital. During this same period, 104 young women with severe symptoms have been selected from the general dispensary for referral to the special functional bleeding clinic. Thus, only about one case in seven was severe enough symptomatically or in the proper age group to require conservative therapy other than curettage.

2. When 104 cases of functional uterine bleeding were classified according to the endometrial diagnosis of the original curettings, 66 per cent were hyperplastic, 16 per cent interval nonsecretory, 12 per cent secretory, and the remaining 6 per cent were chronic endometritis and atrophic types.

3. A total of 234 curettements was done on these 104 patients. Sixty-three per cent of the repeated curettages performed for a recurrence of symptoms showed no change in the endometrial pattern. Of the remaining 36 per cent of patients who showed a variation in pattern, none of the untreated varied from the nonsecretory type to secretory.

The patients showing endometrial hyperplasia and other types of nonsecretory endometrium were clinically similar and on subsequent curettages showed the endometrial patterns to be mutually interchangeable. For this reason, no differentiation has been made between these groups in the evaluation of therapy.

4. Seventy-four of the 91 patients showing nonsecretory endometrium were considered suitable for cyclic progesterogen therapy in that they constituted a group of young women with severe symptoms which did not respond to other forms of treatment. In 72 cases, the bleeding symptoms were satisfactorily controlled. A patient with an ovarian neoplasm and another with gonorrheal cervicitis and an associated pelvic inflammatory disease failed to respond to therapy. Thirty-one patients had no recurrence of symptoms following the initial three-month cyclic course of medication. Sixteen of these thirty-one patients had no adjunctive therapy. Recurrences which occurred in forty patients were successfully treated again with progesterone.

5. Oral progeninolone has been as satisfactory as intramuscular progesterone in the present series, in approximately 90 per cent of the patients.

6. Estrogen has been used in conjunction with progesterone only in the two cases of bleeding associated with an atrophic type of endometrium.

7. There were thirteen cases showing secretory endometrium and originally considered to be truly functional in type. Of these, however, only four proved to have uncomplicated functional bleeding. These cases had a disturbance in the menstrual interval. In the other nine cases there were prolonged, profuse, but regular menses, although some of these had spotting during the menstrual interval. Six patients in this group showing secretory endometrium were treated with progesterone and none responded to therapy. It has been assumed, therefore, that although progesterogen therapy is excellent in functional bleeding associated with nonsecretory endometrium, it is unsatisfactory in those patients who have abnormal bleeding associated with secretory endometrial patterns.

We wish to express our appreciation to Roche-Organon, Inc. for supplying us with the Progestoral necessary for this study.

References

1. Jones, G. E. Seegar, and Te Linde, R. W.: Bull. Johns Hopkins Hosp. **71**: 282, 1942.
2. Jones, H. W.: Am. J. Obst. & Gynec. **35**: 64, 1938.

FACTORS INFLUENCING THE RAT OVARY HYPEREMIA REACTION AS A TEST FOR PREGNANCY

PAUL H. FRIED, M.D., PHILADELPHIA, PA.

(From the Department of Obstetrics and Gynecology, Jefferson Medical College and Hospital, and the Endocrine Division of the Hospital Laboratories)

THE present study was undertaken to evaluate the controversial factors which have been found to influence the accuracy of the rat ovary hyperemia reaction, with particular regard to the diagnosis of pregnancy. The differences in accuracy between the favorable[3, 7, 9-17, 4] and unfavorable reports[2, 5, 8, 1] were considered to be due to variances in test procedure. In the favorable reports, as well, the test routine varied and there were diverse opinions on the effect of the various factors in the test material and procedure on the accuracy of the reaction.

Procedure and Methods

Studies were performed on a series of 517 urine specimens sent to the Endocrine Laboratories of the Jefferson Hospital for the two-hour rat ovary hyperemia pregnancy test. The test procedure basically was as follows: immature albino rats of a Wistar strain, 26 to 32 days old and 45 to 60 Gm. in weight, were injected intraperitoneally with 2 c.c. of urine, were killed in two hours by ether asphyxiation, and autopsied. The rat ovary hyperemia reaction was negative if the ovaries were pale or pinkish. The reaction or test was positive if one or more ovaries were hyperemic, being light to dark crimson in color, without consideration of ovarian enlargement or follicle changes.

The investigation included such factors in the test animals as age, weight, strain, and number; the factors in the urine specimen, as albumin, pH, temperature, hormones, cloudiness, specific gravity, and bacteria; the factors in the administration of the urine, as injection site, number of injections, and dosage; the factors in asphyxiation as asphyxiating agent, optimum time for asphyxiation; and the factors in the autopsy as optimum time for autopsy after asphyxiation, autopsy technique, color intensity, and reading. For comparative studies, the minimal effective dosage* (M.E.D.) of chorionic gonadotrophin† for the hyperemia reaction at two hours was determined and found to be 0.6 International Unit. Positive reactions were present in 76 per cent of the 50 rats injected with this dosage which paralleled the reaction accuracy (77 per cent) noted by us with normal pregnancy urines at two hours. More than 2,000 rats were used for this investigation.

Results and Discussion

The Test Animals.—The weights in the favorable reports were either of a wide range, 30 to 80 Gm.,[11] a limited range, 35 to 40 Gm.,[14] or specific, 50 Gm.[7] The ages were from 18 to 55 days. In this series, the best weight was found to be 45 to 60 Gm., and the best age from 26 to 32 days (Table I).

*The minimal effective dosages were considered to be the smallest amount to produce positive ovary hyperemia reactions in approximately 75 per cent of five or more rats.

†A. P. L. (Ayerst, McKenna, and Harrison).

TABLE I. RELATIONSHIP OF WEIGHTS OF RATS TO THE ACCURACY OF THE RAT OVARY HYPEREMIA REACTION

WEIGHT OF RATS (GM.)	NO. OF PREGNANCY URINES	NO. OF RATS	NO. OF FALSE NEGATIVE REACTIONS	ACCURACY PER CENT
31-35	32	64	23	74.0
36-45	83	166	39	76.5
46-50	168	336	45	81.0

In the recent favorable reports, one[14] or two[7, 11, 14] rats have been used. In this study three rats per test were necessary for the greatest accuracy (Table II).

TABLE II. RELATIONSHIP OF THE NUMBER OF RATS USED PER TEST TO THE ACCURACY OF THE RAT OVARY PREGNANCY TEST

NO. RATS PER TEST	NO. PREGNANCY URINES	NO. FALSE NEGATIVE TESTS	ACCURACY PER CENT
1	56	10	82.2
2	33	2	94.0
3	15*	0	100.0

*Ectopic pregnancies.

Preparation of the Urine Specimen.—The amount of urine injected by others depended upon the specific gravity,[10] was increased for daytime specimens,[7, 9, 11] or the urine was rejected if the specific gravity was less than 1.010[14] or 1.012.[2] Filtration of all urines[10] or of cloudy urines alone,[9] the use of only clear urines,[14] or centrifuging of urines to remove sediment[7] have been advocated as well. In this study there was a slight increase in the number of false negative reactions after the use of clouded urines with a high specific gravity which apparently retarded urine absorption (Table III). Of note in our series were two cases of pregnancy in which the urine specific gravities were 1.003 and 1.004. One was a ruptured ectopic pregnancy and the other was an early normal pregnancy in which the urine specimen was collected five days after the expected date of the first missed menses. The ovarian reactions were strongly positive in the four animals injected.

TABLE III. RELATIONSHIP OF SPECIFIC GRAVITY OF PREGNANCY URINES TO THE ACCURACY OF THE RAT OVARY HYPEREMIA REACTION AND PREGNANCY TEST

SPECIFIC GRAVITY OF URINE	NO. PREGNANCY URINES	NO. RATS	FALSE-NEGATIVE REACTIONS	FALSE NEGATIVE TESTS
1.000-1.010	10	20	2	0
1.011-1.020	40	80	10	1
1.021-1.030	48	96	16	3
1.031-1.040	14	28	6	2

Kline[10] reported that urines of nonpregnant patients with slight traces of albumin may cause doubtful reactions while Ramsey et al.[14] urged that the urine be free of albumin. In this study, the urines of nonpregnant patients with one to four plus albumin were injected alone, while in another group of rats subminimal doses of chorionic gonadotrophin, 0.3 International Units, were added to the nonpregnant urines with four plus albumin (Table IV). The ovarian reactions were negative, being pale in color.

TABLE IV. EFFECT OF ALBUMIN IN NONPREGNANCY URINE UPON THE RAT OVARIAN HYPEREMIA REACTION

AMOUNT ALBUMIN*	NO. URINE SPECIMENS	CHORIONIC GONADOTROPHIN (I.U.)	NO. RATS	NEGATIVE REACTION
0	2	0	10	10
1	4	0	8	8
2	1	0	2	2
4	10	0	20	20
4	4	0.3	5	5

*Grade 1 plus to 4 plus by the Exton method.

A neutral or acid urine has been recommended for injection.[9, 14] In this study, pregnancy urines or the M.E.D. of chorionic gonadotrophin were injected with an adjusted pH of 5.0 or 7.0. The ovarian reaction accuracies were similar (Table V).

TABLE V. EFFECT OF PH OF PREGNANCY URINE AND CHORIONIC GONADOTROPHIN ON THE ACCURACY OF THE RAT OVARY HYPEREMIA REACTION

pH	NO. RATS INJECTED WITH PREGNANCY URINES	NO. RATS INJECTED WITH 0.6 I.U. CHORIONIC GONADOTROPHIN*	FALSE NEGATIVE REACTIONS
5.0	194	–	26
	–	10	3
7.0	194	–	29
	–	10	3

*Minimal Effective Dosage—which was that amount which produced positive rat ovary hyperemia reactions in approximately 75 per cent of five or more rats.

It has been suggested that the urine be injected at room temperature[7] or after heating to a temperature of 35° C. or 38° C.[9] In this study, the urines of pregnant and nonpregnant women were injected at 36° C., 12° C., and room temperature while the M.E.D. of chorionic gonadotrophin was injected at 36° C. and 12° C. (Table VI). There was no notable variance in the accuracy of ovarian reaction. At 36° C. there was a slight increase in fluid retention in the abdominal cavity.

TABLE VI. EFFECT OF TEMPERATURE OF URINE AND CHORIONIC GONADOTROPHIN ON THE RAT OVARY HYPEREMIA REACTION AND URINE ABSORPTION

TEMPERATURE DEGREES C.	NUMBER URINES*	NUMBER RATS	FALSE NEGATIVE REACTIONS	FREE FLUID IN ABDOMINAL CAVITY			
				NONE	SLIGHT	MODERATE	MARKED
36	11	11	2	4	2	3	2
12	11	11	1	8	1	2	0
Room	11	11	1	6	3	2	0
36	Chorionic Gonadotrophin 0.6 I.U.†	6	1	6	0	0	0
12		6	1	6	0	0	0

*Six pregnancy and five non-pregnancy urines.
†Minimal effective dosage.

Rejection[10, 14] or detoxification[9] of urines contaminated with bacteria has been considered necessary. In this study, the percentage of toxic reactions was 0.8 after the injection of 2 c.c. of urine and 21.7 with 5 c.c. of urine

(Table IX). Though a number of the urines were contaminated with bacteria, the three urines which were toxic in 2 c.c. doses were free of bacteria but contained penicillin which had been given to the patient prophylactically.

Farris[6] noted an occasional positive reaction after the injection of estrogens while Kline[10] reported that estrogens in the urine of nonpregnant women may cause doubtful reactions. In this study, an aqueous suspension of estrone sulfate was injected into 10 rats in doses of 5,000 to 40,000 International units, while progesterone in an aqueous suspension* was injected into 8 rats in doses of 5 mg. All reactions were negative.

Kupperman and Greenblatt[11] indicated that the ovary hyperemia reaction is dependent upon the luteinizing or luteotrophic gonadotrophins and cannot be induced by the follicle-stimulating gonadotrophin. Farris[6] found that ovary hyperemia was produced by pure anterior pituitary hormones as the follicle-stimulating hormone (McShan), the luteinizing hormone (Gurin), and the follicle-stimulating synergist (Schering). The ovarian hyperemia reaction was elicited in this study by the following gonadotrophins: sheep or horse pituitary, chorionic, lactogenic (luteotrophic), and pregnant mares' serum. The relative activity of each was noted (Table VII). In addition, Zondek et al.[1] and Farris[5, 6] reported false positive rat ovary hyperemia pregnancy tests upon the injection of urines with a high content of follicle-stimulating hormone (menopause, fibroids, midinterval of the cycle of patients with normal menses). In this study, the two-hour rapid rat pregnancy test was performed with the urine of these types of cases and with the urines of lactating postpartum (tenth day) patients in which high levels of lactogenic hormone, and low levels of chorionic gonadotrophin may be expected (Table VIII). In the "mideycle" and amenorrhea cases, 2 c.c. of the urine gonadotrophin assay extract were also used. The reactions to the urines and gonadotrophin extracts were negative with one exception.

TABLE VII. MINIMAL EFFECTIVE AMOUNTS OF GONADOTROPHINS EVOKING THE RAT OVARY HYPEREMIA REACTION

GONADOTROPHIN	M.E.D.[1]
Whole pituitary	
Equine pituitary[2]	0.3 R.U.
Gonadophysin[3]	0.5 R.U.
Pituitary synergist[4]	0.155 U.
Chorionic	
Korotrin[5]	0.60 I.U.
Follutein[6]	0.55 I.U.
Antuitrins[7]	0.65 I.U.
A.P.L.[8]	0.60 I.U.
Pregnant Mares' Serum	
Anteron[9]	2.5 I.U.

[1]Minimal effective dose. That amount which produced positive rat ovary hyperemia reactions in approximately 75 per cent of five or more rats.

[2]Squibb.

[3]Searle.

[4]Kindly furnished by Dr. Erwin Schwenk of Schering Corporation. Made from sheep pituitaries and is chiefly follicle-stimulating hormone with traces of luteinizing hormone.

[5]Winthrop.

[6]Squibb.

[7]Parke, Davis & Co.

[8]Ayerst, McKenna, and Harrison.

[9]Schering.

*Kindly furnished by Dr. Erwin Schwenk of Schering Corporation.

TABLE VIII. EFFECT OF SPECIFIC NONPREGNANT URINES AND URINE GONADOTROPHIN CONCENTRATES UPON THE RAT OVARY HYPEREMIA REACTION

DIAGNOSIS	URINE[1, 2] NUMBER OF CASES	URINE[1, 2] REACTIONS POSITIVE	URINE[1, 2] REACTIONS NEGATIVE	URINE GONADOTROPHIN CONCENTRATE[1, 3] NUMBER OF CASES	URINE GONADOTROPHIN CONCENTRATE[1, 3] REACTIONS POSITIVE	URINE GONADOTROPHIN CONCENTRATE[1, 3] REACTIONS NEGATIVE	GONADOTROPHIN ASSAY (M.U. PER 24 HOURS)
Midcycle[4]	20	0	40	12	2[7]	22	12-196
Amenorrhea[5]	10	0	20	5	0	10	102 to over 196
Fibroids	10	0	20	-	-	-	-
Postpartum[6]	12	0	24	-	-	-	-

[1]Two rats injected per specimen.

[2]Two c.c. of a 12 or 24-hour specimen collected for gonadotrophin assay.

[3]Two c.c. of the urine gonadotrophin extract (alcohol-ether-acetone extraction) dissolved in 12 c.c. of distilled water represented 1/24th of the total 24-hour output of gonadotrophins.

[4]Midcycle time and ovulation determined by temperature chart and endometrial biopsy.

[5]Menopause and primary ovarian deficiency.

[6]Lactating. Ten days post partum.

[7]Same patient. Unconcentrated urine was not injected. Pregnancy occurred during that menstrual cycle. Corpora hemorrhagica and lutea in mice injected for gonadotrophin assay which was over 196 M. U. per 24 hours.

Factors in the Administration of the Urine.—The amount of urine injected by the advocates of this test has varied from 2[11, 17] to 10 c.c.[7] Salmon and his group[17] used from 1 to 8 c.c. without an appreciable effect in ovarian reaction accuracy. In this study, 2 c.c. of urine injected intraperitoneally were considered to be the optimum dose after the evaluation of the series of rat ovary hyperemic pregnancy cases in which 2 or 5 c.c. were injected (Table IX). The accuracy of the ovarian reactions was the same.

TABLE IX. RELATIONSHIP OF THE AMOUNT OF INJECTED PREGNANCY URINE TO THE ACCURACY OF THE RAT OVARY HYPEREMIA REACTION

AMOUNT (C.C.)	TYPE OF PREGNANCY	NUMBER OF RATS*	FALSE NEGATIVE	ACCURACY PER CENT	TOXIC REACTIONS
2.0[a]	Normal	242	35	85.4	3
	Disturbed	110	26	77.0	
5.0[b]	Normal	164	28	83.0	50[c]
	Disturbed	66	16	76.0	

*Two rats injected with each urine. a. Intraperitoneally. b. 2 c.c. intraperitoneally. 3 c.c. subcutaneously. c. Not toxic in 2 c.c. doses.

Kupperman and Greenblatt[11] advised that 2 c.c. of urine be injected intraperitoneally in two divided doses to facilitate the absorption of urine and produce a sharper point. In this study, in 371 cases, 2 c.c. of urine were injected intraperitoneally in single and divided doses without a notable difference in ovarian reaction accuracy. This was corroborated when 2 c.c. of each of ten pregnant women's urine was injected into twenty rats in single and divided doses (Table X). With the latter urine absorption was slightly less.

TABLE X. EFFECT OF SINGLE AND DIVIDED INTRAPERITONEAL INJECTIONS OF PREGNANCY URINE UPON THE OVARY ABSORPTION AND HYPEREMIA REACTION

	NO. RATS	URINE IN ABDOMEN NONE	URINE IN ABDOMEN SLIGHT	URINE IN ABDOMEN MODERATE	URINE IN ABDOMEN MARKED	POSITIVE REACTIONS STRONG	POSITIVE REACTIONS MODERATE	POSITIVE REACTIONS WEAK
Single*	10	7	2	1	0	5	4	1
Divided†	10	5	3	2	0	4	4	2

*Two c.c. lower midabdomen.

†One c.c. into each of the right and left lower quadrants.

A particularly controversial point in the performance of the two-hour rat pregnancy test is the best route of injection, subcutaneous or intraperitoneal. Kupperman and Greenblatt[11] noted a 99.5 per cent accuracy with the intraperitoneal route and a 65 per cent accuracy with the subcutaneous avenue of injection. They were of the opinion that the high percentage of inaccurate results obtained by Zondek et al.[1] (31.5 per cent errors in normal pregnancy) and Farris[5] were due to the use of the subcutaneous rather than the intraperitoneal route of injection. Salmon,[16] however, reported a 95 per cent accuracy with the subcutaneous injection. In this study, the minimal ef-

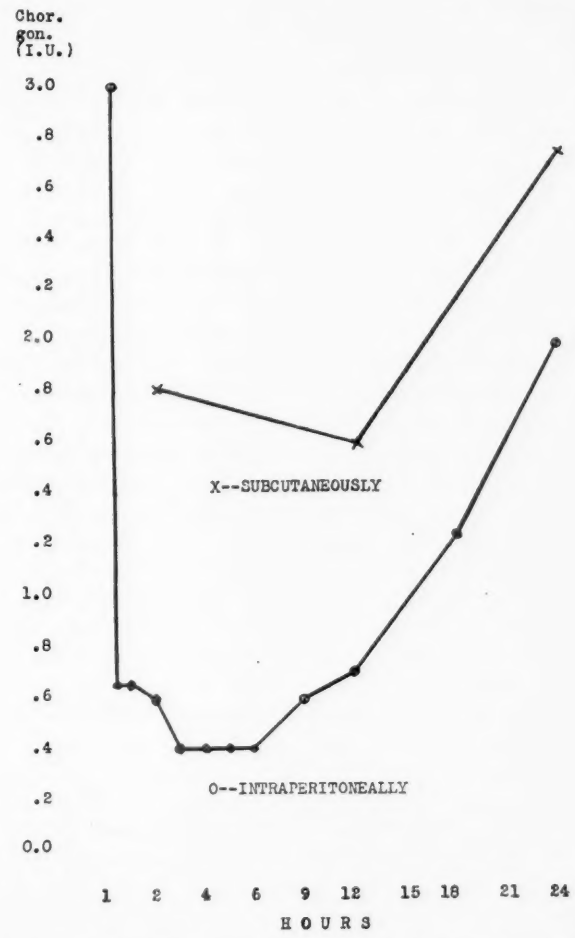


Fig. 1.—Minimal dosage* of chorionic gonadotrophin at various time levels on basis of rat ovary hyperemia reaction.

fective dosage of chorionic gonadotrophin injected subcutaneously and intraperitoneally was determined and compared at two, twelve, and twenty-four hours (Fig. 1). At these time levels, the subcutaneous doses were much higher than the corresponding intraperitoneal dosages. Moreover, when the minimal intraperitoneal dose of chorionic gonadotrophin at two hours, 0.6 International units, was injected into 12 rats intraperitoneally and 12 rats subcutaneously, positive ovarian hyperemia reactions were noted in 75 per cent of the former and 25 per cent of the latter.

*Positive reaction noted in 75 per cent or more of five or more rats. Not noted are the 10 and 30 minute intraperitoneal doses, 50 and 18 units.

Asphyxiation.—In the various reports on the rapid rat pregnancy test, the optimum time for asphyxiation after injection has varied from two to thirty hours. Zondek et al.[1] reported the accuracy of the subcutaneous test to be greatest at twenty-four hours, least at two hours, and intermediate at six hours. Salmon and his group[17] noted the six-hour subcutaneous test to be slightly more accurate than the two-hour test and to be more striking than the twelve and twenty-four hour tests. Others[10, 14] found the six-hour test with subcutaneous injections to be the most reliable. Bunde[2] estimated the two-hour intraperitoneal test to be more accurate than the six-hour subcutaneous test, while Kupperman and Greenblatt[11] considered them to be equally accurate. Fried,[8] in a small series, judged the two- and six-hour intraperitoneal tests to be equally accurate. It has been stated that tests can be read at thirty hours[16] or thirty-six to forty-eight hours[11] after injection. The ovary hyperemia reaction with chorionic gonadotrophin is reported to begin in two hours and reach its peak in twenty-four hours.[1] In this study, in determining the optimum time for asphyxiation after injection, the minimal effective dosage of chorionic gonadotrophin was noted at various time levels (Fig. 1). The smallest M.E.D. was noted at three to six hours, which, therefore, were the times of maximum effect. The M.E.D. was slightly increased at one and one-quarter, two, nine, and twelve hours, and the accuracy with the pregnancy test may be about the same as at the times of maximum effect. However, before one and one-quarter and after twelve hours the results may be much less accurate with pregnancy urines of comparatively low gonadotrophin content, since the M.E.D. rose sharply at these time levels. The earliest time reaction was at ten minutes.

The asphyxiating agents recommended have been ether, illuminating gas, and chloroform. Ether as the asphyxiating agent was found to be very satisfactory since the hyperemic ovaries stood out in good contrast to the pale uteri and oviducts. Since illuminating gas causes a varying hyperemia of the tissues, due largely to the formation of carboxyhemoglobin, consideration was given this asphyxiating agent to increase the sharpness of the positive end point. In this study, ether and illuminating gas were sued to asphyxiate the control rats as well as the animals injected with urines of menopausal women and nonpregnant normally menstruating women collected at the midcycle. The ovarian reactions of the rats asphyxiated with ether were "negative" while some "positive" reactions occurred after asphyxiation with illuminating gas (Table XI). Farris,[5] who used illuminating gas, reported the two-hour rapid rat pregnancy test to be inaccurate because of the large number of false positive reactions in menopausal and normal nonpregnant women at the midinterval of the cycle. Salmon[16] stated that illuminating gas in some parts of the country may cause a hyperemia of the rat ovary in which case the use of ether is advisable.

TABLE XI. HYPEREMIA EFFECT UPON THE OVARY PRODUCED BY ASPHYXIATING AGENTS

	ASPHYXIATING AGENTS			
	ETHER		ILLUMINATING GAS	
URINE*	POSITIVE	NEGATIVE	POSITIVE	NEGATIVE
Menopausal†	0	12	6§	6
Midcycle‡	0	12	3§	9
Controls	0	3	3	0

*Two c.c. injected into each rat.

†Urine gonadotrophins, 102 to over 196 mouse units per 24 hours in the three patients.

‡Midcycle and ovulation determined by temperature chart. Urine gonadotrophin, 12 to 96 mouse units per 24 hours in the three patients.

§After two minutes three were pale negative, five were borderline negative pink, and one remained positive.

Autopsy.—Autopsy has been advised immediately after asphyxiation and also five minutes after the animals are placed in the death chamber.[10, 14, 17] In this study, five of seven rats were injected intraperitoneally with 0.6 to 20.0 International units of chronic gonadotrophin. After two hours the rats were anesthetized with ether and the ovaries were immediately exposed. The normally pink color of the ovaries was increased in the injected, anesthetized rats, dependent upon the dose of injected chorionic gonadotrophin. The ovaries were then observed during and after ether asphyxiation. As the point of asphyxiation approached, all ovaries blanched and at death were completely pale. The control ovaries remained pale. In the injected rats the time necessary for the ovarian color change from "death paleness" to a positive crimson was dependent upon the dose of chorionic gonadotrophin and the final degree of color, ranging from three minutes for the minimal to one minute for the larger amounts of chorionic gonadotrophin.

The technique of autopsy is important. Bleeding in the region of the ovaries has been considered a significant factor since it may cloud the reading.[11, 17] In this study, three rats were injected with 1 International unit of chorionic gonadotrophin, asphyxiated with ether in two hours, and autopsied. The ovarian reactions were positive. A small incision in the liver or abdominal blood vessels caused moderate bleeding and incited almost immediate blanching of the hyperemic ovaries. Irritation of the ovaries during inspection also blanched hyperemic ovaries. The amount of irritation necessary was directly proportional to the degree of color.

To increase the color intensity at autopsy it has been advised that traction be applied to the uterus and ovary[10] or that the ovaries in situ be exposed to the atmosphere for five minutes.[16] In this investigation, traction to the uterus either increased or decreased the color intensity, while exposure to air intensified the color of doubtful and positive reaction. In 316 cases, five doubtful reactions were intensified to weak positive reactions after five minutes of exposure. Since three of the five rats had been injected with urines of nonpregnant women, three reactions were false positives. Kline[10] recommended immediate reading of the ovaries after autopsy since exposure may intensify the color of the ovaries and may add to the confusion in borderline cases.

The necessary features of a positive rat ovary hyperemia reaction as a test for pregnancy have been variously reported. In 4 per cent of the positive reactions only the left of the two ovaries was hyperemic. The left ovary frequently was more hyperemic than the right ovary. Enlargement of the ovary at two hours was infrequent and was not essential for a positive reading as considered in reports on the six hour and other tests. Hyperemia of the follicles alone was not sufficient for a positive reading. In a few cases, after the injection of urine from nonpregnant women or of subminimal doses of chorionic gonadotrophin, or after the use of illuminating gas, a borderline positive or a doubtful reaction was noted which faded within two minutes to a negative reaction.

Comparison of the Two-Hour and Three-Hour Tests.—A three-hour rapid rat ovary hyperemia pregnancy test was performed by the technique evolved by this study on each of 200 specimens of urine sent to the Endocrine Laboratory of the Jefferson Hospital by 200 ward, clinic, and private cases for a rapid rat pregnancy test. The results were compared on the basis of ultimate clinical diagnosis and Friedman tests with those of a reported series of 200 two-hour rat pregnancy tests[8] in which the technique of test performance was that advised by Kupperman and Greenblatt.[11] The two techniques varied in time, number of injections, autopsy routine, and specific weight and ages of the test animals. The number and types of pregnancy cases were the same

in the two series. Three rats were used in a number of cases in the two-hour test while two rats were used in all of the three-hour tests. The two and three-hour rat tests were similar in accuracy (Table XII). Since the rapid rat pregnancy test has not been accepted by some as a routine laboratory test because of the large number of false negative reactions and lack of a sharp positive end point,[2, 8, 1] the two procedures were also compared on this basis. The number of false negative reactions was less in the three-hour test than in the two-hour test (Table XII). Moreover, the end point of the positive reactions in the three-hour test was slightly more pronounced.

TABLE XII. COMPARISON OF PREGNANCY TESTS

PREGNANCY TEST	PREGNANCIES				NONPREGNANT		FALSE NEG. REACTIONS
	NORMAL		DISTURBED				
	POS.	NEG.	POS.	NEG.	POS.	NEG.	
Three-hour rat ovary hyperemia	81	3	20	10*	1	84	37 (16%)
Two-hour rat ovary hyperemia	83	4	24	11	0	78	60 (27%)
Friedman rabbit	114	5	26	26†	3	159	–

*One false negative.
†Four false negative.

The number of false negative reactions, though lowered, still was high in the three-hour test and apparently was not due to factors in the test performance. From the data in a series of 316 cases, it was apparent that approximately 95 per cent of the negative and doubtful reactions in pregnancy cases were due to individual animal variation. That is, there was variation in ability to absorb the injected urine or, if absorption occurred, the ability to react to the absorbed gonadotrophin. For corroboration, the following experiments were performed. Two c.c. of urine of each of two pregnant women were injected intraperitoneally into each of two rats. Each urine evoked one positive and one negative reaction. There was no urine in the abdominal cavities of two rats of which one was positive and the other negative. The latter was considered as a "nonreactor." Of the other two rats, 0.4 c.c. of urine was present in the abdominal cavity of the positively reacting rat and 1.3 c.c. in the negative rat. The 1.3 c.c. of urine were aspirated and were injected intraperitoneally into another rat. A strong positive reaction resulted. The latter negative reaction was attributed to poor absorption of the urine. This study was repeated with other urines with similar results. The largest number (90 per cent approximately) of the false negative reactions in a series of 316 cases with the modified technique was due to "nonreacting" rats, since the urine was completely absorbed. Further investigation is necessary to decrease the number of false negative reactions and to increase the sharpness of the positive end point.

Summary and Conclusions

Differences in the test procedure of the rapid rat pregnancy test have been considered the basis for the disparity in accuracy between the favorable and unfavorable reports; the inaccuracies in the latter were largely due to false negative reactions. Moreover, there has been a difference in opinion on the effects of certain factors in the urine, such as albumin, pH, temperature, hormones, cloudiness, specific gravity, and bacteria, as well as

details of technique, such as injection site, dosage, number of injections, asphyxiating agent, optimum asphyxiation time, autopsy technique, and reading. These controversial factors were evaluated in this investigation in order to develop a test procedure which offered the maximum accuracy. This was done on a consecutive series of 517 urine specimens.

The technique found to be most satisfactory was as follows: Three 26- to 32-day-old, 45 to 60 Gm., female albino rats of the Wistar strain are used. Two c.c. of an unaltered urine, except for filtration if cloudiness is present, are injected intraperitoneally in a single dose. The rats are asphyxiated in three hours (not later than six) with ether preferable to illuminating gas as the asphyxiating agent. Autopsy is performed about three minutes after the death of the animals with particular care to avoid hemorrhage and ovarian irritation. The ovaries are examined immediately. A satisfactory end point is the presence of a distinct ovarian hyperemia, light to dark crimson in color as compared to pale or pinkish controls, in one or more of the ovaries examined, without regard to the color of individual follicles or ovarian enlargement. The results with this three-hour rapid rat pregnancy test were favorable. Although the two- and three-hour rat pregnancy tests were approximately similar in accuracy (96.7 and 96.5 per cent, respectively) the number of animals giving false negative reactions in the three-hour test was decreased (from 27 to 16 per cent of rats injected with pregnancy urines). The other major difficulty which had been encountered in the rapid rat pregnancy test was the lack of a sharp positive end point, which too was improved slightly with the three-hour test. Further investigation is necessary to decrease the number of false negative reactions and to increase the sharpness of the positive end point.

References

1. Zondek, B., Sulman, F., and Black, R.: J. A. M. A. **128:** 939-933, 1945.
2. Bunde, C. A.: Am. J. Obst. & Gynec. **53:** 317-320, 1947.
3. Eberson, F., and Silverberg, M. H.: J. A. M. A. **96:** 2176-2182, 1931.
4. Walker, T. F., and Walker, D. V. H.: J. A. M. A. **111:** 1460, 1948.
5. Farris, E. J.: Am. J. Obst. & Gynec. **48:** 200-207, 1944.
6. Farris, E. J.: Am. J. Obst. & Gynec. **52:** 14-27, 1946.
7. Frank, R. T., and Berman, R. L.: Am. J. Obst. & Gynec. **32:** 492-496, 1941.
8. Fried, P. H.: Am. J. Obst. & Gynec. **54:** 689-693, 1947.
   Fried, P. H.: West. J. Surg. **56:** 552, 1948.
9. Kelso, R. E.: Am. J. Clin. Path. **10:** 293-299, 1940.
10. Kline, B. S.: Am. J. Clin. Path. **14:** 557-562, 1944.
11. Kupperman, H. S., and Greenblatt, R. B.: South. M. J. **39:** 158-165, 1946.
12. Kupperman, H. S., and Greenblatt, R. B.: Bull. Univ. Hosp. (Augusta, Ga.) **5:** 6-16, 1944.
13. Kupperman, H. S., and Greenblatt, R. B., and Noback, C. R.: J. Clin. Endocrinol. **3:** 548-550, 1943.
14. Ramsey, T. L., Falkenstein, A. P., and Seykowski, E. J.: J. Lab. & Clin. Med. **29:** 419-428, 1944.
15. Reiprich, W.: Klin. Wchnschr. **12:** 1441-1444, 1933.
16. Salmon, U. J.: Personal communication, Jan. 10, 1947.
17. Salmon, U. J., Geist, S. H., Salmon, A. A., and Frank, I. L.: J. Clin. Endocrinol. **2:** 167-170, 1942.

1812 Spruce Street

PRIMARY AND SECONDARY SPONTANEOUS HABITUAL ABORTION

CARL T. JAVERT, M.D., WILLIAM F. FINN, M.D., AND
HENRICUS J. STANDER, M.D.,* NEW YORK, N. Y.

(From the Department of Obstetrics and Gynecology, Cornell University Medical College, and the Woman's Clinic of the New York Hospital)

HABITUAL abortion is a disturbing obstetric problem with an obscure etiology. Many investigators have employed prophylactic therapy with this and that vitamin, hormone, and method of treatment and have drawn conclusions regarding the etiology from the results of treatment. It has been difficult to comprehend the good results obtained by the empirical use of only one agent or mode of therapy. Perhaps additional measures were employed unwittingly and not appraised statistically. There has been no general agreement as to the definition of habitual abortion and some studies include patients who have had only one or two abortions. Could faulty selection of patients be responsible for the high percentage of successful pregnancies irrespective of the treatment employed? The present study was undertaken in 1940 against this background. It has several objectives: first, to define habitual abortion; second, to determine the incidence; third, to detect as many of the contributing factors, defects, and deficiencies as possible; and, finally, to evaluate the results obtained by correcting these conditions.

Definitions

An abortion is defined for the purpose of this study as a pregnancy ending at or before the twenty-second week of gestation and resulting in a fetus weighing 500 Gm. or less.

"Primary habitual abortion" is used to classify obstetric patients who have had three or more consecutive spontaneous abortions beginning with the first pregnancy.

"Secondary habitual abortion" designates those who have had three or more consecutive spontaneous abortions following delivery of one or more immature, premature, or full-term infants.

The definition of abortion given above was prompted by the following circumstances:

1. Consideration of fetuses on the basis of weight and duration of pregnancy has provided our Pathological Laboratory with a suitable description of an abortus.

2. In keeping with the Clinic policy of regarding a premature infant as weighing from 1,501 to 2,500 Gm., and a full-term infant as weighing over 2,500 Gm., it seemed proper to classify infants weighing from 501 to 1,500 Gm. as immature, and fetuses weighing 500 grams and less as abortuses.

3. The *Quarterly Bulletin of the New York City Department of Health* states that twenty cities require registration of stillbirths having twenty-two weeks or more gestation, while the United States Public Health Service bases its stillbirth statistics on a uterogestation of twenty weeks and over.

*Died May 2, 1948.

4. Streeter has shown that a gestation of twenty-two weeks produces a fetus weighing approximately 500 Gm.

5. No fetus weighing less than 500 Gm. has ever survived at the New York Hospital. However, according to Levine, there have been 32 survivals in infants weighing between 501 and 1,000 Gm.

It would appear from this evidence that the time-honored practice of considering premature labors of 28 weeks or less as a miscarriage, or an abortion, is in need of downward revision. These infants have survived and become classified as "living abortions," a rather undesirable term. Accordingly, in keeping with what has been said above, a practical classification of infants on the basis of weight and duration of pregnancy at the time of delivery is presented herewith:

CLASSIFICATION OF INFANTS ACCORDING TO WEIGHT AND DURATION OF PREGNANCY AT THE TIME OF DELIVERY

CLASSIFICATION	BIRTH WEIGHT (GM.)	DURATION OF PREGNANCY (WEEKS)
Abortus	0-500	0-22
Immature	501-1,500	22-30
Premature	1,501-2,500	30-36
Full Term	2,501 and over	36-40

Present Study

Incidence.—This study covers a 15-year period (1933 to 1947) during which time 56,803 pregnancies were cared for at the Woman's Clinic of the New York Hospital. Statistical tables are offered telling a tale not always referred to in the text. Table I shows that 123 patients with primary habitual abortion were treated in 189 pregnancies, giving an incidence of 1:300. Sixteen did not return in a subsequent pregnancy. The highest number of consecutive abortions per patient was 11, the lowest 3, while the average number per patient was 4.2. There were 88 patients in the secondary abortion group who were studied in 115 pregnancies, giving an incidence of 1:493. The highest number of consecutive abortions was 10, the lowest 3, while the average per patient was 4.5. The definitions stated above were rigidly adhered to in the selection of patients for this study.

TABLE I. PRIMARY AND SECONDARY HABITUAL ABORTION

	TOTAL NUMBER OF PATIENTS	TOTAL NUMBER OF PREGNANCIES	TOTAL NUMER OF PREGNANCIES AT WOMAN'S CLINIC (1933-1947)		INCIDENCE
			HABITUAL ABORTION PATIENTS	TOTAL CLINIC POPULATION	
Primary abortion	123	669	189	56,803	1:300
Secondary abortion	88	679	115	56,803	1:493
Grand total	211	1348	304		

Obstetrical Performance.—The primary group had a total of 669 pregnancies; the secondary group had 679, making a grand total of 1,348 for analysis. The obstetrical history of each group *before* and *after* classification can be obtained at a glance from Tables II and III. The primary group had a total uncorrected abortion rate of 76.5 per cent and 57.4 per cent for the secondary group of patients. Both are considerably higher than the prevalent rate of 10 per cent for the entire clinic population. The immature, premature, and full-term salvage is also given in these tables; the latter is only 20.1 per cent and 39.6 per cent for the primary and secondary groups, respectively, whereas for the entire clinic it is over 80 per cent.

TABLE II. PRIMARY HABITUAL ABORTION. OBSTETRICAL PERFORMANCE BEFORE AND AFTER CLASSIFICATION REGARDLESS OF THERAPY

	ABORTION		IMMATURE		PREMATURE		FULL TERM		
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	TOTAL
Before	369	100.0	0		0		0		369
After	142	47.3	14		9		135	45	300
Total (uncorrected) performance	511	76.5	14	2.1	9	1.3	135	20.1	669

TABLE III. SECONDARY HABITUAL ABORTION. OBSTETRICAL PERFORMANCE BEFORE AND AFTER CLASSIFICATION REGARDLESS OF THERAPY

	ABORTION		IMMATURE		PREMATURE		FULL TERM		
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	TOTAL
Before	295	62.3	0		9		169	35.7	473
After	95	46.1	3		8		100	48.5	206
Total (uncorrected) performance	390	57.4	3	0.5	17	2.5	269	39.6	679

A part of this study is devoted to an evaluation of results with treatment; therefore, it is necessary to determine the obstetrical outcome without treatment. This was done for each pregnancy *after* classification as shown in Tables IV and V. The total average abortion rate does not vary significantly from any of the individual pregnancies and was 65.0 per cent and 46.5 per cent for the two groups, respectively, with a full-term salvage rate of 26.4 per cent and 47.7 per cent. Full-term expectancy was somewhat better in the secondary group, which must be taken into consideration when evaluating results from any method of therapy. It is realized that a parallel series with and without treatment would be more systematic. However, Tables IV and V will be used as controls and will be referred to again as Type I therapy in Tables X and XI.

TABLE IV. PRIMARY HABITUAL ABORTION. OBSTETRICAL HISTORY AFTER CLASSIFICATION ACCORDING TO PREGNANCY WITHOUT THERAPY

PREGNANCY SEQUENCE	ABORTION		IMMATURE		PREMATURE		FULL TERM		
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	TOTAL
First	48	61.5	6		3		21	26.9	78
Second	35	67.3	2		2		13	25.0	52
Third	16	66.6	2		–		6	37.5	24
Fourth	11	84.6	–		–		2	15.3	13
Fifth	9	66.6	–		1		2	22.2	9
Sixth and Over	7	53.8	–		–		6	47.2	13
Total (uncorrected) performance	123	65.0	10	5.3	6	3.1	50	26.4	189

TABLE V. SECONDARY HABITUAL ABORTION. OBSTETRICAL HISTORY AFTER CLASSIFICATION ACCORDING TO PREGNANCY WITHOUT THERAPY

PREGNANCY SEQUENCE	ABORTION		IMMATURE		PREMATURE		FULL TERM		
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	TOTAL
First	38	53.5	1		5		27	38.0	71
Second	17	44.7	1		1		19	50.0	38
Third	6	35.2	–		1		10	58.8	17
Fourth	3	30.0	–		–		7	70.0	10
Fifth	2	28.4	–		–		5	71.6	7
Sixth and Over	9	50.0	–		–		9	50.0	18
Total (uncorrected) performance	75	46.5	2	1.2	7	4.3	77	47.7	161

Clinical and Laboratory Data.—A complete history, physical examination, and certain laboratory determinations were performed on each patient. The pertinent data are presented in Tables VI and VII. Control incidences obtained from annual reports, publications, and individual studies of the department, are provided as available for ready comparison. It is readily apparent that both the primary and secondary groups of habitual abortion patients had similar contributing factors, defects, and deficiencies. This confirmed a suspicion that no single cause was responsible and at the same time indicated that secondary abortion patients should receive more serious consideration. While they have already demonstrated ability to have one or more children and, therefore, have a better prognosis as to full-term expectancy without treatment than the primary group, it is even better with specific measures. However, this advantage is offset by a much higher infantile mortality rate, as will be shown in Table XIV. While dietary information is lacking for the entire series of patients, one finds evidence of improper nutrition in the incidence of anemia, vitamins C and K deficiency. Blood loss from recurrent abortion may explain some of the cases with anemia. More specific data in this regard were obtained from a study of a separate group of 33 primary abortion patients and are provided in Tables XII and XIII.

TABLE VI. CLINICAL DATA ON PATIENTS WITH PRIMARY AND SECONDARY HABITUAL ABORTION

DATA	PRIMARY ABORTION	SECONDARY ABORTION	CONTROL
No. of patients	123	88	--
Race: White	93 per cent	92 per cent	88 per cent
Negro	7 per cent	8 per cent	12 per cent
Average age	31 years	31 years	23 years
Elderly primiparas (Over 35 years)	25 per cent	--	8 per cent
Gynecologic complications	60 per cent	52 per cent	--
Medical complications	4 per cent	9 per cent	--
Second husband	3 per cent	1 per cent	--

TABLE VII. LABORATORY DATA ACCORDING TO NUMBER OF PREGNANCIES IN PRIMARY AND SECONDARY ABORTION

DATA	PRIMARY ABORTION NO.	PRIMARY ABORTION PER CENT	SECONDARY ABORTION NO.	SECONDARY ABORTION PER CENT	CONTROL
Number of pregnancies	189		115		56,803
Wassermann	(175)		(105)		
Positive		6		7	2.0 per cent
Hemoglobin below 70 per cent	(139)	15	(89)	17	7.0 per cent
Rh Factor:	(40)		(28)		
Positive		83		88	85.0 per cent
Negative		17		12	15.0 per cent
Basal metabolism:	(28)		(6)		
Minus value		65		50	--
Vitamin C concentration*	(44)		(11)		
(Below 0.5 mg. per cent)		55		45	50.0 per cent
Prothrombin concentration†	(26)		(8)		
(Below 70 per cent of normal)		47		22	15.0 per cent
Modified prothrombin test‡	(14)		(3)		
(Below 70 per cent of normal)		0		0	1.0 per cent

(Figures in parentheses indicate number of patients studied.)
*Mindlin and Butler Technique.
†Warner, Brinkhous, and Smith.
‡Summerson-Bonsnes.

Obstetrical Complications.—The occurrence of the same complications of pregnancy in either group as shown in Table VIII is of obstetrical interest. Nausea and vomiting occurred frequently, and served to reduce the value of an adequate antepartum diet, and were more pernicious when the patient's nutrition

was poor to start with. Evidence of nutritional deficiency was found in many patients when specific laboratory tests were made. As will be emphasized in Table XIII, some of these patients manifested a hemorrhagic diathesis consisting of bleeding from the nose, gums, and anus, as well as facile bruising of the skin, in addition to vaginal bleeding. Threatened abortion had a higher incidence and may be indicative of a partial or marginal separation of the placenta, as in the case recently reported by Javert. Deficiency in vitamin C or K may be responsible for decidual bleeding which predisposes the patient to premature separation. Rutherford has found evidence of abnormal decidual bleeding in patients with threatened abortion by means of histological studies of decidual biopsies. Such a symptom-complex of bleeding is suggestive of deficiency in the anti-hemorrhagic vitamins C and K, which was partially confirmed by laboratory tests, especially with regard to "C."

Placenta previa had a much higher incidence in the habitual abortion in patients. Patients with threatened abortion were also found by Stander to have this complication with greater frequency. Recently, two uteri were observed following hysterectomy in the first trimester of pregnancy and one contained a central placenta previa and the other a marginal one. Ordinarily, placenta previa and premature separation of the placenta are seldom mentioned as causes for spontaneous abortion.

The data on premature rupture of the membranes are incomplete. Not infrequently, these patients have a leakage of fluid per vaginam in the fourth or fifth month of gestation. One can often obtain a history of prior intercourse under such circumstances. Accordingly, complete abstinence from coitus during the entire pregnancy has been part of the treatment. Coitus may also result in stimulation of uterine contractions and be undesirable for that reason.

TABLE VIII. OBSTETRIC COMPLICATIONS IN PATIENTS WITH PRIMARY AND SECONDARY ABORTION

COMPLICATION	PRIMARY ABORTION		SECONDARY ABORTION		CONTROL
	NO.	PER CENT	NO.	PER CENT	
Total no. of pregnancies	189		115		56,803
Nausea and vomiting	166	87	70	60	33.0 per cent
Toxemia of pregnancy	13	7	11	9	5.0 per cent
Threatened abortion	28	15	8	7	0.9 per cent
Placenta previa	8	4	2	2	0.3 per cent
Premature rupture membranes	10	5	6	5	30.0 per cent

Gynecological Complications.—It seemed pertinent to consider the various kinds of gynecological disease because of a possible role in the pathogenesis of habitual abortion. A summary of the various conditions is presented in Table IX. Retroversion had a much higher incidence than in a control series of 100 parous and 100 nonparous women. Perhaps some of the patients had a spontaneous correction with or without the aid of the knee chest position. Correction of persistent retroversion has usually been accomplished by the combined technique described by Javert. When this gave unsatisfactory results, and when the uterus was adherent, a suspension operation was performed, and other complications were also corrected at the same time. Two patients developed primary habitual abortion after uterine suspension and are therefore of special interest. Several patients had a myomectomy because of fibromyomas. The obstetrical results following uterine suspension and myomectomy were as follows:

	SUSPENSION		MYOMECTOMY	
	ABORTION	FULL TERM	ABORTION	FULL TERM
Primary habitual abortion	2	7	2	5
Secondary habitual abortion	3	4	2	3
Total	5	11	4	8
Incidence (per cent)	31	69	33	66

Three patients had a double uterus. Curettings of five patients revealed cervical and endometrial polyps. Contrary to expectation, lacerated cervices and amputations were of minor importance in the secondary group, which is in agreement with the findings of Finn regarding the influence of cervical operations on subsequent childbearing.

TABLE IX. GYNECOLOGICAL COMPLICATIONS AND TYPE OF TREATMENT IN PATIENTS WITH HABITUAL ABORTION

	NUMBER OF PATIENTS			NUMBER OF PATIENTS	
COMPLICATIONS	PRIMARY (123)	SECONDARY (88)	TREATMENT	PRIMARY (123)	SECONDARY (88)
Uterus:					
Retroversion uteri	50	30	Pessary	11	0
			Suspension	10	3
Myoma uteri	11	7	Myomectomy	3	2
Double uterus	2	1	None		
Cervical laceration	–	2	Repair	–	1
amputation	–	1			
Descensus uteri	–	2	None		
Polyps, cervical	3	–	Polypectomy	3	–
endometrial	1	–	Curettage	1	–
Ovary:					
Ovarian cyst	3	2	Oophorocystectomy	1	1
			Cyst resection	2	1
Salpinx:					
Salpingitis	3	–	Salpingectomy	3	–
Ectopic pregnancy	1	1	Salpingectomy	1	1
Total number	74	46		34	8
Total incidence	60 per cent	52 per cent		28 per cent	9 per cent

Summary of Treatment.—The obstetric outcome of 280 pregnancies in 107 primary habitual abortion patients, and of 209 pregnancies in 88 secondary abortion patients is shown in Tables X and XI. The various types of treatment employed can be divided approximately as follows:

Type I. No Treatment. This control group of patients have been presented in Tables IV and V. They received essentially no therapy since they had aborted, were threatening to abort, or did so immediately after consulting a physician.

Type II. Empirical Treatment. This designates former therapy which was based on practical observations and accepted procedure without specific study of individual patient requirements. It includes prenatal care, complete or partial bed rest, restriction of coitus at the time of the expected menstrual period, sedation, vitamin E, progesterone, thyroid extract, and antisyphilitic therapy.

Type III. Rational Treatment. This implies specific detection and correction of certain factors, defects, and deficiencies, and represents the current treatment. It consists of antenatal care; diets high in citrus fruits, fresh vegetables, and minerals, dietary supplements including vitamin C (50 to 100 mg., three times a day), K (5 mg. daily) and minerals; complete restriction of coitus; psychotherapy; avoidance of mineral oil (which absorbs the fat-soluble vitamins); and thyroid extract when the basal metabolism rate is low. Bed rest and sedation are reserved for those with threatened abortion. Some patients also received vitamin E and progesterone, but these agents are no longer employed.

The obstetric outcome according to the various types of treatment described above has been summarized in Tables X and XI. Type III therapy gave the best results as shown by an abortion rate of only 14 per cent as contrasted with 65 per cent in the control group without treatment. It provided a corresponding increase in the full-term salvage, which was 26 per cent in the control patients and 80 per cent after Type III treatment. Current therapy also gave

promising results in seven patients with secondary habitual abortion. Insufficient consideration had been given to this group on the erroneous assumption that they needed no special consideration inasmuch as they had already born a viable child. This accounts for the small number of patients in the secondary group.

TABLE X. PRIMARY HABITUAL ABORTION. OBSTETRICAL OUTCOME FOLLOWING VARIOUS TYPES OF TREATMENT COMPARED WITH CONTROL

THERAPY	NUMBER OF PREGNANCIES	ABORTION		IMMATURE		PREMATURE		FULL TERM	
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Type I (control) See Table IV	189	123	65.0	10	5.3	6	3.1	50	26.4
Type II	50	13	26.0	4		1		32	64.0
Type III	41	6	14.6	0		2		33	80.4
Total	280								

TABLE XI. SECONDARY HABITUAL ABORTION. OBSTETRICAL OUTCOME FOLLOWING VARIOUS TYPES OF TREATMENT COMPARED WITH CONTROL

THERAPY	NUMBER OF PREGNANCIES	ABORTION		IMMATURE		PREMATURE		FULL TERM	
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Type I (control) See Table V	161	75	46.5	2	1.2	7	4.3	77	47.7
Type II	41	19	46.3	1		1		20	47.5
Type III	7	0		0		0		7	100.0
Total	209								

Special Clinic

A special clinic was established in 1940 for the study of habitual abortion and for the standardization of management and treatment. The contemplated program was interrupted by World War II so that, finally, only 33 patients had been uniformly studied and treated in 41 pregnancies. Data on these patients have been presented in Tables X and XI. Additional information pertaining to them is provided in Tables XII and XIII. Multiple factors, defects, and deficiencies were diagnosed and treated. Occasionally, after an abortion, corrective measures were instituted before the next pregnancy. Urological examinations were performed on nine husbands and normal spermatozoa were found in all. Two patients remarried and went to term in the very next pregnancy with Type III treatment.

Gradually vitamin E and progesterone therapy were discontinued with the following results:

	NO. OF CASES	ABORTIONS	PREMATURE AND FULL TERM
With progesterone	21	2	19
Without progesterone	20	1	19
With vitamin E	28	6	22
Without vitamin E	13	2	11

Virtually the same results were obtained with vitamin E and progesterone as without them. This led to a withholding of vitamins C and K in certain patients with primary habitual abortion with the following results:

With vitamin C	41	6	35
Without vitamin C	2	2	–
With vitamin K	33	7	26
Without vitamin K	11	1	10

TABLE XII. PRIMARY HABITUAL ABORTION. SUMMARY OF CONDITIONS FOUND IN 33 PATIENTS BEFORE RECEIVING TYPE III THERAPY

CONDITION	NUMBER	PER CENT
Nutrition inadequate	27	82
Nausea and vomiting	23	70
Bed rest and sedation	30	90
Coitus in pregnancy	28	85
Psychomatic instability	28	85
Mineral oil used	15	45
Gynecological complications	19	57
Dietary deficiencies: vitamin C	17	51
prothrombin (K)	14	42
Hormone deficiency: minus basal metabolism rate	17	51
Medical complications: hemorrhagic diathesis	22	66
underweight, overweight	8	24
anemia, positive serology	6	18
Total	254, or average of 7.7 per patient	

TABLE XIII. PRIMARY HABITUAL ABORTION. SUMMARY OF TYPE III THERAPY EMPLOYED IN 41 PREGNANCIES

TREATMENT	NUMBER	PER CENT
Nutritional instructions	41	100
Nausea and vomiting control	25	61
Bed rest and sedation omitted	37	90
Coitus prohibited	41	100
Psychomatic therapy	41	100
Mineral oil prohibited	41	100
Gynecologic complications corrected	17	41
Dietary supplements: vitamin C	38	92
vitamin K	30	73
vitamin E*	28	68
minerals	18	43
Hormone supplements: progesterone	21	51
thyroid extract	17	41
Medical complications treated	14	34

It would appear that vitamin C gave slightly better results than did vitamin K, though more data are needed to arrive at any definite conclusions. However, in a separate series of patients with threatened and spontaneous abortion, vitamin C deficiency was found in nearly three-fourths of the patients.

Gradually, after omitting various agents and methods from the therapy, one may ultimately discover which procedure is responsible for the favorable results and thereby ascertain the pathogenesis of habitual abortion. At the present time, one must conclude that there are several causative factors and several remedial agents and procedures. Among the latter are vitamin C, sexual abstinence, and psychotherapy.

Psychosomatic Obstetrics

Perhaps nowhere in the field of medicine does one encounter as many emotionally unstable patients as in cases where there is no offspring. The docility and equanimity of the usual obstetric patient are lacking. The habitual abortion patients are apprehensive, fearful, and cry easily. Physicians have endeavored to console them by stating that nature has deliberately cast off an abnormal child. This serves to increase a guilt complex that is invariably present. They always ask: "Why do I abort?" Sometimes they add: "My husband says it is my fault." In days gone by, the Puritans interpreted miscarriage as signifying intercourse on a holy day. It would be interesting to know their reasons for this point of view.

Nervous tension and anxiety may result in nausea and vomiting as shown in Table XIV. Such loss of food substances can reduce the value of a normal diet and exert a greater effect on those with a poor nutrition. Dietary deficiencies were corrected, and vitamin and mineral supplements were provided. Perhaps in some patients such treatment also served as a placebo. Continuation of activity was insisted upon in order to keep the patient occupied, while bed rest was reserved for those with threatened abortion. There is no actual proof that constant bed rest is essential for a successful confinement since most women have a satisfactory termination without it.

TABLE XIV. TYPE OF DELIVERY (PREMATURE AND FULL TERM), CONGENITAL ANOMALIES, MATERNAL AND INFANTILE MORTALITY IN HABITUAL ABORTION

DELIVERY	PRIMARY ABORTION		SECONDARY ABORTION		CLINIC INCIDENCE (PER CENT)
	NO.	PER CENT	NO.	PER CENT	
Spontaneous	95	67.9	96	88.0	85
Operative:					15
Forceps	27	19.0	5	5.0	
Caesarean section	15	10.6	1	1.0	
Breech extraction	5	3.5	5	5.0	
Version	0		1	1.0	
Total number	142		108		
Congenital anomalies	3	2.0	1	1.0	2.9
Maternal mortality	2	1.4	1	1.0	0.2
Infantile mortality	5	3.5	13	12.0	3.0

At first it seemed wrong to advise these patients to conceive again and again. However, this point of view was confirmed by the actual results. A spirit of rivalry and improvement of morale replaced their previous downheartedness as they observed one another continuing successfully to term. The nursing and social services rendered valuable assistance to many patients. Some were advised to seek spiritual comfort at prayer and from the church. While psychotherapy is a necessary part of the treatment, it is most difficult to evaluate its importance statistically.

Type of Delivery and Congenital Anomalies

When a patient reaches full term after many recurrent abortions, the initial joy is replaced by apprehension of labor. Under such circumstances, analgesia is indicated and spontaneous delivery is anticipated, as shown in Table XIV. Cesarean section had a higher incidence in the primary group.

Congenital anomalies had a lower incidence in each group of patients than ordinarily occurs in the clinic population. Malpas reported a rate of 2.9 per cent, which is also extremely low. Accordingly, there appears to be no basis for stating that these patients should avoid future pregnancies.

Maternal and Infantile Mortality

Two maternal deaths followed cesarean section and one occurred after a midforceps delivery as shown in Table XIV. The infantile mortality rate in the primary group was the same as that for the clinic, but it was four times greater in the secondary abortion patients. This demonstrates the need for an increased interest and effort in the management of this type of patient even though she has a better prognosis as to full-term expectancy.

Discussion

This study had a fourfold purpose, namely, to define habitual abortion, to determine the incidence, to detect the contributing factors, defects, and de-

ficiencies, and to evaluate the results obtained by the correction of these conditions. The histories, physical examination, and laboratory determinations revealed multiple conditions which were essentially the same in both groups of primary or secondary habitual abortion patients. These patients were rigidly classified even though it means losing a good many who had fetuses just over 500 Gm. Multiple therapeutic agents or methods were employed with gratifying results as shown by the reduction of the abortion rate from 65 per cent to 14 per cent, with a corresponding increase in the full-term salvage from 26 per cent to 80 per cent. However, it is equally important to mention five primary abortion patients who had 7, 8, 9, 10, and 12 consecutive abortions, respectively, and never succeeded in reaching viability. Several of these have since adopted children.

Unfortunately, it is difficult to assess the individual merit of any single agent or method. Gradually, certain items such as vitamin E and progesterone were eliminated without noticeable impairment of the end results. Similarly, vitamin K has been omitted from the treatment given to ten patients who went to term. While these agents corrected an underlying deficiency, they may have had also a placebo effect. Therefore, it is equally difficult to evaluate the benefits of psychotherapy.

Some light may have fallen on the pathogenesis of habitual abortion. Lack of antihemorrhagic vitamin C and possible K may precipitate decidual bleeding leading to premature separation of the placenta and ultimate spontaneous abortion. Certain patients showed evidence of hemorrhagic diathesis as manifested by nasal, gingival, rectal, and dermal bleeding in addition to vaginal bleeding of threatened abortion. Many of these patients had low values for ascorbic acid in blood plasma and others were also low in prothrombin concentration. Moore et al. have concluded that vitamin K deficiency was a factor in producing abortion in rabbits.

There is such a maze of literature that proper cognizance cannot be taken of all of the pertinent articles. As the reader reviews them in order to develop his own philosophy, let him be reminded of three important matters: the high percentage of success irrespective of which vitamin, hormone, or method is employed; the lack of specific information as to the pathogenesis of human spontaneous abortion.

It is of interest to review the treatment of habitual abortion at the Woman's Clinic since its establishment in September, 1932. At that time, it was the usual practice to employ empirical treatment based on clinical experience and observation. Complete bed rest was insisted upon, and intercourse was permitted or interdicted only at the time of the expected menstrual period. Thyroid extract was in vogue, and antisyphilitic therapy was occasionally recommended on the history of recurrent abortion. The advent of the Wassermann test put a stop to indiscriminate antisyphilitic therapy. Little or no attention was paid to diet, nutrition, and anemia.

The first patient to receive nutritional consideration of habitual abortion was placed on a high-vitamin, high-iron diet by one of us (C.T.J.) in 1936. This patient was delivered of a full-term child after having sustained three previous

abortions. Vitamin E and progesterone were introduced and great reliance was placed on these agents. Not infrequently, the habitual abortion patients were referred to the Sterility Clinic for appraisal of their problem, even though none of them exhibited any particular difficulty in becoming pregnant.

A Special Clinic was established in 1940 for the study and treatment of habitual abortion. Patients made regular antenatal visits and various tests and determinations were obtained, as tabulated in Tables XII and XIII. Meanwhile, vitamin K had engaged the interest of obstetricians with regard to hemorrhagic disease of the newborn. Together with vitamin C, it became the subject of an investigation reported by Javert and Stander. This focused attention on the importance of the nutritional aspects of habitual abortion and certain dietary supplements were administered according to individual patient requirement. The Warner, Brinkhous, and Smith test was used for the plasma prothrombin determinations and at first many low values were obtained and reported. This test, as modified by Summerson and Bonsnes, now reveals normal prothrombin values in habitual abortion. This led to the discontinuance of vitamin K therapy in ten patients who had a satisfactory outcome. However, because of insufficient data, this vitamin is still employed in our present regimen. By a gradual elimination of all agents and methods, one may ultimately discover the pathogenesis of habitual abortion. Unfortunately, certain circumstances required that the Special Clinic be discontinued in September, 1947, so that clinical management of these patients has reverted to the use of Type III therapy on an empirical basis with a continuation of the good results.

Conclusions

1. A patient having three or more consecutive spontaneous abortions beginning with the first pregnancy is regarded as having "primary habitual abortion."

2. A patient is designated as having "secondary habitual abortion" when three or more consecutive abortions follow delivery of one or more immature, premature, or full-term infants.

3. An abortion is rigidly defined as a pregnancy ending at 22 weeks' gestation or less and resulting in a fetus weighing 500 Gm. or less.

4. The incidence of primary habitual abortion is 1:300 and for the secondary variety it is 1:493.

5. One hundred twenty-three primary habitual abortion patients had 669 pregnancies, and 88 secondary abortion patients had 679 pregnancies, making 1,348 in all for analysis.

6. The uncorrected abortion rate without treatment was 65 per cent for the primary group, and 46 per cent for the secondary group of patients with a corresponding full-term expectancy of 26 per cent and 47 per cent, respectively, showing a somewhat better prognosis for the secondary habitual abortion patient. This was offset in part by an infantile mortality rate of 12 per cent for these patients.

7. The histories, physical examinations, and laboratory determinations of both the primary and secondary groups revealed the same multiple factors, defects, and deficiencies.

8. Current therapy is based on the detection and correction of all contributory conditions and consists of dietary instructions, dietary supplements such as vitamins C and K and minerals, abstinence from intercourse, continued ambulation and activity, psychotherapy, thyroid extract as indicated, elimination of gynecologic disease, and avoidance of mineral oil.

9. The above regimen yielded a full-term salvage of 80 per cent in the primary group and 100 per cent in the secondary group with a corresponding reduction in the primary abortion rate to 14 per cent.

10. It is impossible to state which vitamin, hormone, or method was responsible for the good results. Elimination of vitamins E, K, and progesterone from the regimen did not seem to impair the outcome.

11. Vitamin C deficiency may predispose to the production of decidual bleeding (threatened abortion) and to premature separation of the placenta and ultimate spontaneous abortion.

12. Coitus in pregnancy may precipitate abortion in predisposed patients.

13. Threatened abortion (premature separation) and placenta previa had an increased incidence in the habitual abortion patients.

References

1. Bonsnes, R.: Personal communication.
2. Finn, W. F.: Am. J. Obst. & Gynec. 56: 291, 1948.
3. Javert, C. T., and Stander, H. J.: Surg., Gynec. & Obst. 76: 115, 1943.
4. Javert, C. T.: Am. J. Obst. & Gynec. 52: 865, 1946.
5. Javert, C. T.: Westchester M. Bull. 15: 11, 1947.
6. Levine, S. Z.: Personal communication.
7. Malpas, P.: J. Obst. & Gynaec. Brit. Emp. 45: 932, 1938.
8. Moore, R. A., Bittinger, I., Miller, M. L., and Hellman, L. M.: Am. J. Obst. & Gynec. 43: 1007, 1942.
9. Rutherford, R. N.: Surg., Gynec. & Obst. 74: 1139, 1942.
10. Stander, H. J.: Am. J. Obst. & Gynec. 44: 531, 1942.
11. Stander, H. J.: Textbook of Obstetrics, New York, 1945, D. Appleton-Century Co., p. 129.
12. Streeter, G. L.: Carnegie Institute, Wash. Publ. 274.
13. Quarterly Bull. Dept. Health. N. Y. Vol. XV, No. 2, June, 1947.
14. U. S. Pub. Health Ser. Vital Statistics, 1945; Vol. 26, No. 1, April, 1947.

PERITONEAL BODIES AND CYSTS OF THE BROAD LIGAMENT*†

R. R. Greene, M.D., B. M. Peckham, M.D., and G. H. Gardner, M.D.,
Chicago, Ill.

(From the Department of Obstetrics and Gynecology, Northwestern University Medical School, and Wesley Memorial Hospital)

A LENGTHY, detailed, and highly intuitive paper by Walthard, published in 1903, was concerned with epithelial inclusions in the ovary. The majority of his data had to do with germinal epithelium inclusions. In addition, he described two ovaries which contained small solid epithelial bodies, noted that similar structures were found in and under the serosa of the tube, and commented that they may undergo cystic changes in this location.

Nowadays the original subject of Walthard's study has been forgotten but these solid and cystic epithelial structures have been termed Walthard's bodies in many publications, whether they are found in the tube or in the ovary.

The name "Walthard bodies" is inappropriate. In the first place, Walthard was a latecomer in describing them. Second, and of more importance, the use of a man's name for an anatomic or pathologic structure is an objectionable and confusing practice. Terminology should have descriptive or etiological significance. The use of a man's name, no matter how respected, leads to confusion. Consequently, in the material to follow, these structures will be referred to as peritoneal bodies or epithelial knots, and their cystic derivatives as peritoneal cysts.

As previously stated, Walthard was not the first to describe these structures. In 1902, Schickele devoted many pages to this subject, citing ten authors who had previously described or discussed them. In 1903, Robert Meyer mentioned articles devoted to or referring to them by six additional authors. Werth, in 1887, gave the first adequate description and discussion of this subject, according to Meyer. Plaut in 1933 also credits Werth with the first good description of these bodies.

Recently (1946) Reis has discussed these "cell balls" and their cystic derivatives. More recently Moore (1947) considered these structures and their cystic derivatives so rare that he published a report on the findings in one patient. He stated that a total of only 266 cases had been reported in the literature. We have made no attempt to check the accuracy of this claim.

Material

The material was derived from routine slides of one or both salpingo-oophorectomy specimens from 150 patients. In addition, the lateral half of the tube, broad ligament and ovary from 16 patients has been serially sectioned and studied. Routine sections were stained with hematoxylin and eosin; in

*Presented before the Chicago Gynecological Society, March 19, 1948.
†Supported in part by a grant from Ciba Pharmaceutical Products, Inc.

addition, Milligan trichrome and iron hematoxylin with mucicarmine have been used.

Findings.—These solid or cystic structures have been noted in specimens from 78 patients. A total of 58 solid bodies and 78 of their cystic derivatives have been found. These data do not include the findings in two serially sectioned specimens. One surface of one broad ligament and both surfaces of the other were literally covered by these solid or cystic structures. The exact number has not been counted. In the routine tissues the number of solid bodies varied from one to three per specimen. The number of cystic structures varied from one to twelve.

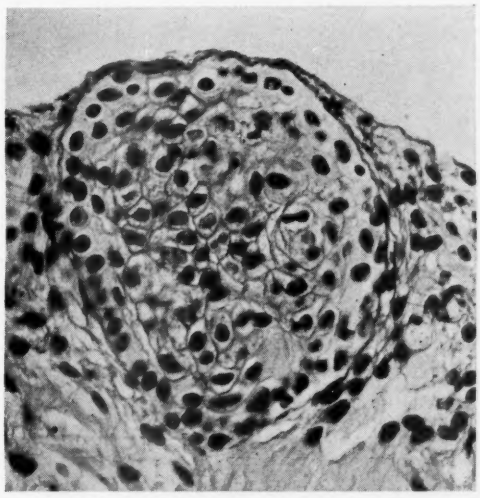


Fig. 1.—Solid epithelial body just under intact serosa of mesosalpinx. Note distinct cell membranes.

Morphology.—The solid bodies (Fig. 1) are composed of a mass of epithelial cells which possess distinct cell membranes, faintly staining cytoplasm and vesicular nuclei with little or no chromatin. As described by Varangot (1938) and D. N. Danforth (1942), there is an infolding of the nuclear membrane. Under oil immersion this infolding frequently gives the nuclei bizarre shapes. There are no intercellular bridges and no basement membrane surrounds the body. There is no true capsule although compression of adjacent connective tissue may give the false impression of a capsule.

The word "squamous" has frequently been used in reference to this epithelium. As pointed out by Ralph Reis, it is not squamous epithelium. There is no flattening of the epithelium either in the solid bodies or in the larger bodies with small cavities. Flattening occurs only when cystic dilatation is fairly extensive.

The process of cavity formation and cystic dilatation can be observed in various specimens. Occasionally, in early cavity formation the immediately adjacent epithelial cells are cuboidal and rarely even columnar (Fig. 2). This appearance, we believe, must be interpreted as a degenerative phenomenon since the nuclei are frequently pyknotic and the cytoplasm of such cells takes on a uniform glassy but deeper stain.

With the accumulation of further fluid, the number of layers of cells in the wall becomes less and the degree of flattening of the cells in the luminal layers becomes greater (Figs. 3 and 4). In the larger cysts the epithelium consists usually of two layers of flattened cells; more rarely, of only a single layer.

Location.—The impression is current that these structures are found only on or just beneath the serosa of the tube. A group of 67 solid or cystic bodies in which the position could be accurately determined was tabulated; 33 were on the tube and 34 on other areas of the broad ligament. In this latter location, nine were on the mesovarium and the remainder (25) on the mesosalpinx.

Fig. 2.—Small cystic body under surface of mesovarium. Note the uniform darker staining cytoplasm and early pyknotic changes in nuclei of cells lining cavity.

It should be noted that most routine blocks were cut to include tube, mesosalpinx, mesovarium and at least part of the ovary. It was thus possible to survey the serosal surface of all the constituents of the broad ligaments in a single section. (In most laboratories, blocks of the tube and ovary are cut separately and the broad ligament is not included. We believe that this is the likely explanation for the current misconception regarding the usual position of these structures.)

Position in Relation to Surface.—The probable mode of development of these structures from peritoneal mesothelium will be discussed later. However, consistent with this histogenesis, a few of the solid bodies showed direct continuity with the mesothelium (Fig. 5). Only a portion of the epithelial mass was therefore subserosal. In other routine specimens, solid bodies and some showing a moderate degree of cystic dilatation were located immediately under but not continuous with the mesothelium. Possibly some of the other solid bodies found in routine sections would have shown continuity with the mesothelium had serial sections been made. In several of the serially sectioned specimens such continuity could be demonstrated. On the other hand, several were observed in the serials that were just subserosal, but there was no continuity with the mesothelium. Still other solid bodies were noted to be separated from the serosal surface by a definite layer of connective tissues (Fig. 6). This

was also true of bodies that showed more than a moderate amount of cystic dilatation. A few of the moderate-sized cysts were entirely below the serosal surface; the majority, however, bulged above the surface level (Figs. 3 & 4). Some were truly sessile or even semipedunculated; this was usually true of the larger cysts.

In a few of the routine sections solid and cystic bodies were apparently deep in the substance of the broad ligament. However, extensive adhesions were present in each instance due either to a previous pelvic inflammatory process or to endometriosis. Consequently, we believe that this location was an artifact, due to distortion of tissues by the coexisting adhesions. Serial sections would probably have demonstrated their near proximity to peritoneal clefts or infoldings. This opinion is neither unique or original. It was expressed by Robert Meyer in 1903.

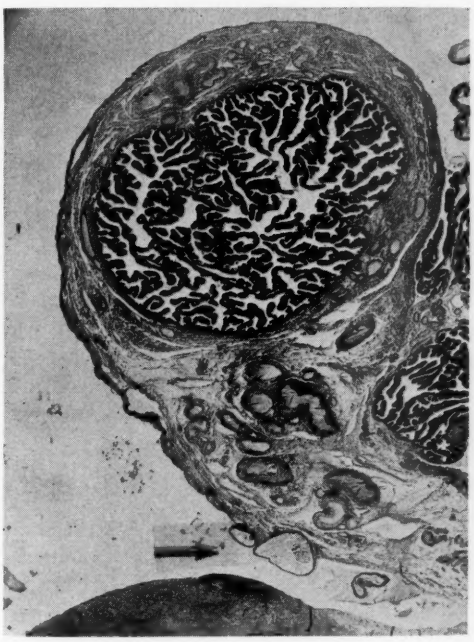


Fig. 3.

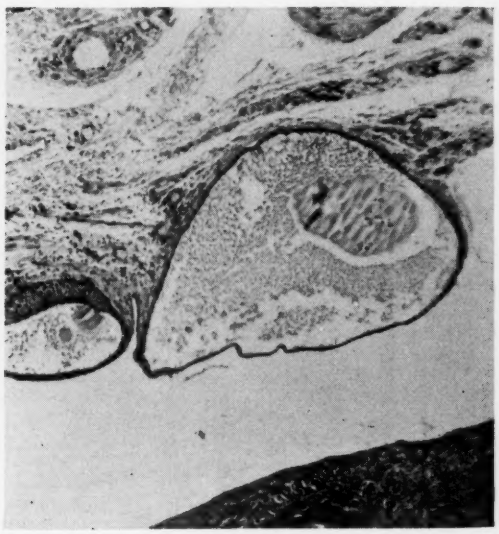


Fig. 4.

Fig. 3.—Low power photomicrograph with arrow pointing to two cystic bodies on surface of mesosalpinx.

Fig. 4.—High power of Fig. 3 showing sessile position of most of the larger cystic body.

Inflammatory Reaction.—Gross pathology reports and microscopic specimens from 35 patients were studied in particular for evidences of present or past inflammatory reactions; it was found in 32 specimens. The microscopic evidence of active inflammatory reaction was quite obvious; it was usually a subacute perisalpingitis associated either with ectopic pregnancies or more frequently with endometriosis. Adhesions alone or in association with other old inflammatory residuals were found in the others. These, too, were associated either with residues of pelvic inflammatory disease or with endometriosis. In the remaining three specimens there was no evidence of present or past inflammatory reaction. It is possible, of course, that such inflammation had occurred in the past but had left no permanent residues.

Differentiation From Cysts of Mesonephric or Paramesonephric Origin.—We have recently presented the detailed histologic characteristics of cysts of the broad ligament derived from the mesonephric duct, mesonephric tubules, and aberrent paramesonephric (tubal or Müllerian) epithelium (Gardner, Greene, and Peckham 1948). In adequate tissue preparations they can be differentiated with certainty from peritoneal bodies and peritoneal cysts. Cysts of mesonephric or paramesonephric origin have a true capsule in which muscular elements can be identified with a Milligan trichrome stain; peritoneal cysts do not have a true capsule. The epithelium of cysts of mesonephric duct origin is single-layered, cuboidal, and has a basement membrane. That of mesonephric tubule origin is more columnar and is composed of two types of cells, lightly staining ciliated cells and more darkly staining nonciliated cells. The epithelium of cysts of paramesonephric origin is identical to that of the oviduct or tube and is composed also of two types of cells, ciliated and secretory. The epithelium of peritoneal cysts on the other hand is composed of flattened cells, usually two layers in thickness.

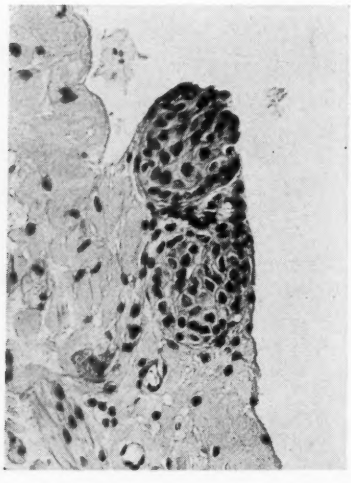


Fig. 5.

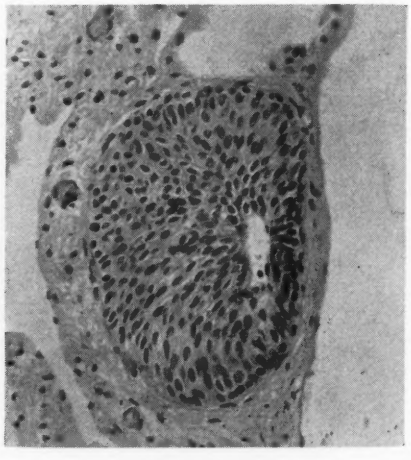


Fig. 6.

Fig. 5.—Two small bodies on surface of uterine tube. One is continuous with peritoneal mesothelium; the other is immediately subserosal.

Fig. 6.—Small epithelial body with minute cavity. It is separated from serosa of mesosalpinx by thin layer of connective tissue.

Histogenesis.—Four main theories have been proposed to explain the histogenesis of peritoneal bodies, the so-called Walthard bodies:

One of the earliest was that these bodies represent or are derived from accessory adrenals. According to Rossa (1898), these solid bodies are accessory adrenal tissue and cysts result from atrophy of this tissue. While accessory adrenals may be found in the broad ligament, their resemblance to these epithelial bodies is indeed slight and most superficial. At present no one holds a brief for this suggested histogenesis.

The second main theory was proposed by Schickele (1902). He believed that they developed *in situ* from surface epithelium. This surface epithelium, however, was not ordinary peritoneal mesothelium but ovarian germinal epithelium which had migrated to this aberrant location in an unknown manner due to an unknown stimulus. The belief that these bodies develop from ovarian germinal epithelium rather than peritoneum seems unnecessarily complicated.

A third theory of histogenesis was added fairly recently by Ralph Reis. He suggested that they developed from misplaced entodermal cells of cloacal origin. His reason for this suggestion was the close similarity of these structures to cell balls of Limbeck and Brunn which are found under the vesical and ureteral mucosa.

This theory seems unlikely. The fact that two structures are morphologically similar does not prove that they have the same embryonic derivation. In fact, while the bladder is largely derived from cloacal entoderm, the ureter where similar cell balls are found is derived from the mesonephric duct—a mesodermal derivative.

A fourth and commonly accepted histogenesis was proposed and well demonstrated by Werth in 1887. He showed that these bodies develop as proliferations of the peritoneal epithelium. He was able to demonstrate continuity in some instances between the epithelial bodies and the overlying serosal epithelium. Various subsequent workers have accepted this mode of development and have also been able to demonstrate similar continuity. In 1903, Robert Meyer published a thorough and most convincing study on this subject. He showed the early stages of proliferation of the peritoneal epithelium and subsequent development of these solid and cystic bodies. His report was based on the findings in solid and cystic structures from 16 specimens. In each case there was evidence of present or past inflammatory reactions. Consequently, he concluded that these bodies occur as a response by the peritoneum to inflammatory processes.

Our findings, particularly in serial sections, are similar to those first described by Werth in 1887, and fully amplified by Meyer. Various stages in the development of these structures have been noted from the early localized areas of proliferation of the mesothelium, the downgrowth of epithelial masses, subserosal masses of epithelial cells no longer connected to the mesothelium, early cystic degenerative changes in the center of these masses and the final end result, peritoneal cysts.

We could find no evidence of present or past inflammatory reaction in three of our specimens. It is possible, however, that these tissues had, in the past, been subjected to a mild inflammatory reaction which had, however, left no permanent residues. It must be remembered that bacterial inflammation is not the only factor that may lead to the development of these structures. That chemical irritation from blood is sufficient to cause their production is evinced by their frequency and easily observed early stages of development, not only with tubal-pregnancy specimens but also in cases of endometriosis. It is even conceivable that they may arise as the result of chemical irritation from a small amount of intraperitoneal bleeding associated with rupture of a follicle. If this were the case, one would not expect to find permanent residues of an inflammatory reaction.

"Walthard Bodies" in the Ovary.—As previously stated, Walthard's original paper was concerned with germinal epithelial inclusions in the ovary. In fact, the solid epithelial bodies given his name constituted only a minor part of his paper. Furthermore, solid epithelial bodies in the ovary similar to those found under the serosa of the tube and broad ligament are very rare in our experience.

In a deliberate study of sections from 100 ovaries, D. N. Danforth found only one solid body of this type, although he found four other cystic derivatives. On the other hand, he found 13 solid and 43 cystic bodies on the tube and mesosalpinx in 350 routine sections.

We found none of these solid bodies and no structures which we could identify as their cystic derivatives in the ovaries of our routine sections. On

the other hand, we found two definite solid epithelial bodies in serial sections (Fig. 7). These were identical in all details with those of the tube and broad ligament. In one specimen direct continuity could be demonstrated with an area of piled up germinal epithelium. The other was directly under the germinal epithelium but separated from it by a thin layer of ovarian stroma. A third specimen in the cortex of an ovary had several solid cords of similar epithelial cells imbedded in a fibrous stroma. This is not included, however, since we are uncertain whether it is, or is not, a true, but minute, "Brenner tumor."

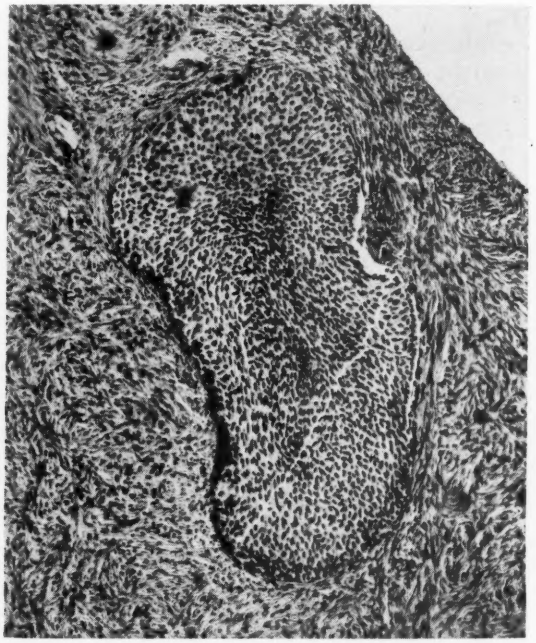


Fig. 7.—Solid epithelial body in cortex of ovary. This specimen showed no continuity with the surface epithelium.

Conclusions

Solid epithelial bodies and their cystic derivatives are found relatively frequently under the serosa of the tube and the broad ligament. The commonly used name "Walthard bodies" is considered inappropriate because personalized nomenclature is confusing and, in regard to priority, Walthard was actually a latecomer in describing these structures.

The solid and cystic structures are found with no greater frequency under the tubal serosa than under the remaining surface of the broad ligament. They are extremely rare in the ovary.

They arise from the peritoneal mesothelium in response to and as part of an inflammatory reaction.

References

1. Danforth, D. N.: Am. J. Obst. & Gynec. 43: 984, 1942.
2. Gardner, G. H., Greene, R. R., and Peckham, B. F.: Am. J. Obst. & Gynec. 55: 917, 1948.
3. Meyer, R.: Virchows Arch. f. path. Anat. 171: 443, 1903.
4. Moore, M. R.: J. Connecticut M. Soc. 11: 619, 1947.
5. Plaut, A.: Arch. f. Gynäk. 153: 97, 1933.

6. Reis, Ralph A.: Am. J. Obst. & Gynec. 52: 964, 1946.
7. Rossa, Emil: Arch. f. Gynäk. 56: 296, 1898.
8. Schickele, G.: Virchows Arch. f. path. Anat. 169: 44, 1902.
9. Varangot, E.: Gynéc. et obst. 38: 11, 1938.
10. Walthard, M.: Ztschr. f. Geburtsh. u. Gynäk. 49: 233, 1903.
11. Werth, E.: Beitr. z. Anat. u. z. operativen Behandl. d. Extrauteringrav. Stuttgart. Stuttgart, 1887.

303 East Chicago Avenue

Discussion

DR. D. N. DANFORTH.—Although there are certain points with which one might differ, this paper is nevertheless one of the major contributions to our knowledge of these minute but fascinating cell masses. Most important, this work shows by the serial section technique the lengths to which they may extend, and their variations. Further, when considered with other work by the same authors, it clarifies the distinction between the cystic nests and the mesonephric and paramesonephric derivatives, which to most of us have been so very confusing.

My own experience with these cellular accumulations is limited for the most part to a study of single routine microscopic sections of 350 normal tubes. Among this material, 56 sections contained cell nests. Thirteen, or 23 per cent, were solid, and the remainder showed cystic change. In this study, my interest was directed almost entirely to the curiously grooved nuclei which are a constant and striking feature of the solid cell masses, and occur with less frequency in the cystic ones. Although similarly marked nuclei occur in many other situations, I have never before or since seen them in such profusion and constancy except in the Brenner tumor of the ovary, of which this nucleus is also a characteristic feature. The chief difference between the material presented tonight and that to which I have just referred is that in one inflammatory changes were a prominent feature, whereas in the other the tissues were normal. In both, the cell bodies are morphologically similar.

The most important conclusion which the essayists make is that the cell masses are inflammatory in origin. The evidence which they present in favor of this thesis is the finding of associated inflammatory conditions in 32 out of 35 cases. In normal tubes, identical rests are considered as a remote effect of inflammation, the inflammatory process having healed, or been subclinical, or subpathological. There is no evidence that in the infected material the nests did not originate before the onset of the associated inflammatory disease for which the adnexa were evidently removed. Also, if the solid nests and plaques, which in our material abound with grooved nuclei, are the form in which these structures originate, it is difficult to relate the appearance of such distinctive tissue to inflammation, either chemical or bacterial, as we know it elsewhere in the body. In fact, all of the classical signs of inflammation are lacking. The serosa of the tube, from which the bodies are said to arise, is similar to the peritoneum which is found throughout the abdomen. If these structures occur in response to inflammation, and especially since they are often visible grossly, would they not be found in abundance elsewhere on the peritoneum, as over the appendix, or gall bladder, or uterus? And would there not be a lingering lymphocyte or polymorphonuclear leucocyte? Further, if, as Meyer and others have postulated, these nests as seen in the ovary are related to Brenner tumors, are these tumors also considered as a response to inflammation? If this were the case, the Brenner tumor would parallel tuboovarian disease in frequency, rather than maintain its place among the rare ovarian tumors.

I have had no occasion to study neonatal or pediatric autopsy material except for the examination of casual specimens. In one of these, a healthy nest, complete with grooved nuclei, was found in the mesosalpinx on routine examination of the adnexa of a 4½-month-old infant. The cause of death in this infant was congenital heart disease, with coarctation of the aorta, cardiac hypertrophy, and pulmonary edema. There was no history or finding of inflammation about the adnexa. For these reasons, although it is possible that associated inflammation may stimulate the proliferation of these structures, I believe that their origin remains obscure.

Finally, I consider the effort to eliminate proper names from anatomical nomenclature to be important and commendable. However, one might object to the suggested term "peritoneal bodies" on the grounds of their admitted occurrence in the ovary, an organ which, strictly speaking, has no peritoneal covering.

DR. RALPH A. REIS.—The essayists report the frequent finding of cell balls or nests in the subserosa of the uterine tube and of the broad ligaments. They emphasize the fact that these cell balls are not made up of squamous epithelium and that they are not the so-called Walthard bodies. With both of these conclusions we are in full accord. Anyone who has studied these cell balls must agree that they are made up of transitional cells.

A study of Walthard's original article will show that he reported on cell rests in the ovary in which the individual cells were made up of nonvesicular nuclei, deep pyknotic cytoplasm, no distinct cell membrane, and were coffee bean shaped as recently emphasized by Danforth. Last, the cell masses are embedded in a network of trabeculated connective tissue. Brenner tumor cells are similar and are likewise embedded in a connective tissue stroma. These differences have been previously emphasized in the discussion of our report of 1946.

A consideration of the etiology of these cell masses raises many interesting questions. The essayists report evidence of inflammation in some 32 and no such evidence in only three specimens. In these latter, they presuppose pre-existing inflammation even though no evidence of such can be found. This conclusion is open to serious question. All the uterine tubes under consideration were removed for cause; therefore inflammation and pathology were found in practically all. In our series, only normal tubes were studied and all tubes showing any evidence of inflammation were carefully excluded. Yet in our study, six out of ten, when studied by serial section, showed these selfsame cell balls. Certainly, then, it would seem that pre-existing inflammation is not necessary and that no one has the right to assume that inflammation must have been present to account for these cell balls.

Furthermore, our studies showed that with the formation of cysts within these cell balls, the transitional cells forming the innermost lining of the cysts assume first low cuboidal, and later high cuboidal shapes while the cells situated peripherally remain transitional in character. We do not agree with the thought that the cells lining the cysts are undergoing a degenerative process.

We are still of the opinion that the change, as first described by Saphir and Kurland, from transitional cells to cuboidal cells, is a reversion to an embryologically younger form of epithelium. It is an excellent example of "dedifferentiation." It has been repeatedly stated that new cells, under the influence of irritation, regeneration, or tumor growth, will undergo a dedifferentiation or reversionary process in the direction of the primary embryonal or blastomere cell. With further growth there is a redifferentiation to form a cell not identical with the original type. This new differentiation results in cells of a lower order of specialization than the original. This is progressive or prosoplastic metaplasia.

Limbeck and Brunn reported similar cell balls with similar cyst formations in the wall of the bladder, the ureter, and the kidney pelvis. Saphir and Kurland found the same structures and were able to trace the development of adenocarcinomas of the bladder to such cell balls. It is, of course, hazardous to conclude similarity of origin from the fact that structures closely resemble each other morphologically. Histologically, cell balls of the urinary tract and of the tube seem similar, and undergo cystic changes in a similar manner.

The clinical significance of these cell balls of the tubal wall lies in the possibility that they may undergo malignant changes as do those of the urinary tract. This question cannot be answered at this time. However, may I recall to you, that we have recorded a primary papillary transitional-cell carcinoma of the uterine tube which probably took its origin from such epithelial cell balls. A second carcinoma was also recorded which consisted of both transitional epithelium and glandular structures. It is possible that this second tumor also arose from such cell balls of the tubal wall.

Finally, the essayists have again emphasized that "terminology should have only descriptive or etiological significance." May I respectfully call their attention to the repeated use of the term "Milligan stain"?

DR. GREENE (Closing).—Dr. Danforth and I have discussed and disagreed on these subjects before. I cannot help but feel that he is overemphasizing the significance of the coffee bean or infolded nucleus. It is found in the so-called "Walthard body" and in the Brenner tumor, but it is also found in many other structures and locations in the body. Such nuclei are common in the germinal epithelium, stromal cells of the ovary, rete epithelium, and medullary cords and tubules of the ovary. They are frequent in the peritoneal mesothelium covering the appendix, the broad ligament, and even in the serosal surface of the uterus. I have seen them in urethral and bladder epithelium, in the cervix in areas of epidermidization and even in a poorly differentiated squamous-cell carcinoma of the cervix where they appeared in profusion.

Concerning the importance of inflammation in the etiology of the peritoneal bodies, we again disagree. In Dr. Danforth's original report on "Walthard bodies," he examined only normal tubes and ovaries. No doubt the endosalpingeal portions of the tubes were normal. However, some of his patients were operated upon for endometriosis. With this latter condition, a mild to moderate perisalpingitis with infiltration with plasma cells and lymphocytes was extremely common in our preparations.

In regard to Dr. Reis' discussion: We stand justifiably rebuked for our own misdemeanor in using "personalized" terminology. He also disagrees as to the etiological importance of inflammation. Perhaps none of us are quite agreed on exactly what are the evidences of past inflammation.

We do not feel too lonesome in our stubborness in this regard. We have good company. In fact our observations are not original but merely agree to what has previously been reported by Robert Meyer and many others.

THE SELECTIVE MANAGEMENT OF PLACENTA PREVIA*

RUSSELL J. PAALMAN, M.D., AND ARTHUR B. HUNT, M.D., ROCHESTER, MINN.

(From the Department of Obstetrics and Gynecology, Mayo Clinic)

PLACENTA previa continues to be one of the more serious complications of pregnancy. Davis and Campbell have estimated that 15 to 20 per cent of the maternal deaths in the country at large are the result of placenta previa, either from severe hemorrhage or from subsequent embolism or infection. There has been some controversy regarding the management of this complication. One group believes that the treatment resolves itself simply into either rupture of the membranes or cesarean section. The other group continues to use the Voorhees bag, the Willett forceps, version, and other methods in treating this condition. This paper is concerned with an analysis of the incidence, treatment, and results obtained in the cases encountered at the Mayo Clinic from 1919 through 1945.

Incidence

The incidence of placenta previa has been reported as ranging from 0.32 to 2 per cent. In the period covered by this study, Jan. 1, 1919, through Dec. 31, 1945, there were approximately 12,000 deliveries on the service of the Department of Obstetrics and Gynecology of the Mayo Clinic in the hospitals of Rochester, Minn. Placenta previa complicated these deliveries 134 times, an incidence of 1.12 per cent, or 1 in 89 deliveries. These 134 cases represent 129 mothers, as 5 patients had one repetition of placenta previa. This incidence of recurrence of this complication is high. Aaberg stated that recurrent placenta previa is an uncommon obstetric complication. He found only two cases of repetition at the Boston Lying-in Hospital from 1925 to 1946. Persall and Torpin also stated that placenta previa seldom occurs in the same patient twice.

Placenta previa has been consistently reported as occurring more frequently in multiparas than in primiparas. In our series 26, or 19 per cent, were in primiparas, and 108, or 81 per cent, were in multiparas. Why multiparas are more subject to this condition is unknown.

Malpresentation is quite common in placenta previa. In our series the incidence was 12 per cent, of which 7.5 per cent represented breech presentations, and 4.5 per cent transverse position. This high incidence was probably the result of the space occupied by the lowlying placenta. Twin pregnancy occurred in 5 per cent, or once in every 19 cases, as compared with a normal of once in 87 pregnancies. A high incidence of placenta previa in twin pregnancy has been noted by other authors,[22] due probably to the fact that the increased surface area of the placenta or placentas increases the chances of low implantation.

We have classified placenta previa into five types: lowlying, lateral, partial, central, and the rare cervical type. This classification[8] is described in detail by Greenhill. The incidence of each type in our series is given in Table I and needs no discussion.

Treatment

General Treatment.—Individualization in each case has been the underlying principle of the management of placenta previa at the clinic. However,

*Read at the meeting of the Minnesota Obstetrical and Gynecological Society, Rochester, Minn., May 1, 1948.

certain general measures are applied in all cases. Preparation for the various obstetric complications is started at the first prenatal visit. In particular, preparations for possible hemorrhage are carried out by determinations of hemoglobin, blood grouping, and Rh factor on each pregnant woman. A large central blood bank, including several bottles of group O, Rh negative blood, makes rapid treatment possible. Although there are plasma, fluids for intravenous use, acacia, and gelatin on hand at all times, whole blood is preferred in the treatment of obstetric hemorrhage.

TABLE I. DISTRIBUTION OF CASES BY TYPE OF PLACENTA PREVIA

	PLACENTA PREVIA, TYPE				
	LOWLYING	LATERAL	PARTIAL	CENTRAL	CERVICAL
Cases	23	9	75	27	0
Per cent	17	7	56	20	0

The house staff is also prepared in advance for obstetric hemorrhage. From the first day of their service the gravity of vaginal bleeding is stressed. Their alertness in getting transfusions and other treatment under way, and in obtaining help from the senior obstetric staff has had a considerable influence on the prognosis for patients with placenta previa.

Painless bleeding in the later weeks of pregnancy should be regarded as arising from placenta previa until proved otherwise. All of the patients with this symptom are hospitalized for study. It is not in the scope of this paper to discuss the differential diagnosis of bleeding in the third trimester. However, circumvallate placenta[12] should be mentioned, as bleeding from this cause may be confused with that from placenta previa; in the literature circumvallate placenta has not received the attention it merits. Table II indicates that almost 80 per cent of the patients with placenta previa show symptoms before term is reached, and 25 per cent actually show symptoms prior to viability of the fetus. Thus, in planning treatment, prematurity becomes an important factor in four cases out of five.

TABLE II. ONSET OF SYMPTOMS*

WEEKS PREGNANT	PLACENTA PREVIA, TYPE				TOTAL	
	LOWLYING	LATERAL	PARTIAL	CENTRAL	CASES	PER CENT
Less than 28	1	1	8	4	14	10
28-29	1	0	5	2	8	6
30-31	4	0	6	2	12	9
32-33	0	1	6	5	12	9
34-35	1	1	9	2	13	10
36-37	5	3	16	5	29	22
38-39	2	2	11	3	18	13
40+	9	1	14	4	28	21

*Twenty-five per cent of symptoms occurred prior to viability, 79 per cent prior to term.

If the bleeding is severe on entry of the patient into the hospital, transfusion is started and the patient is taken directly to the delivery room for vaginal examination. Rectal examinations are avoided on patients with vaginal bleeding. A second room stands ready for cesarean section. Further treatment depends on the result of the vaginal examination and on other factors which will be discussed later.

If on entry of the patient the bleeding is not severe enough to demand immediate attention, a placentogram and a cystogram usually are ordered. These roentgen examinations often give inconclusive results; such results are disregarded. There are, however, a reasonable number in which the placenta can be

visualized satisfactorily. In these patients the placentogram is of distinct help. When it is determined that the placenta is *not* in the zone of dilatation, the patient is examined vaginally to determine the cause of bleeding, and any indicated treatment is instituted.

When placenta previa is diagnosed by placentogram, some method of delivery is selected, as the continuation of pregnancy is often fraught with danger. Hemorrhage can be combatted, but delay only increases the hazards of infection in the presence of vaginal bleeding. In a very small number of carefully selected cases prior to viability of the fetus, vaginal examination is withheld and the patient remains in the hospital until the fetus is large enough to be delivered alive. This is usually done only in situations in which it is of more than usual importance that a living infant be obtained. A roentgenologic diagnosis of placenta previa is of particular help in the management of the condition in these occasional cases.

When the placentogram has not helped in the diagnosis, a vaginal examination is done, a second room being kept ready for section. In spite of improved roentgenologic techniques, vaginal examination remains the only conclusive method of diagnosing placenta previa. Once the obstetrician has committed himself to vaginal examination, treatment is indicated at once, as a delay of a few days markedly increases the risk of infection.

Active Management.—The plan of management in our cases is summarized in Table III. Thirty-seven patients, or 28 per cent, had minimal bleeding and required no treatment.

TABLE III. TYPE OF TREATMENT

TREATMENT, TYPE	PLACENTA PREVIA, TYPE				TOTAL	
	LOW-LYING	LATERAL	PARTIAL	CENTRAL	CASES	PER CENT
No treatment	14	3	20		37	28
Ruptured membranes	7	2	19		28	
Voorhees bag	1	2	14		17	
Version		1	6	3	10	46
Bag and version			4	1	5	
Bag and Willett forceps			1		1	
Bag and breech extraction				1	1	
Cesarean section	1*	1	11†	22	35	26

*Section performed because of hypertension.
†In 2 of the 11 cases, section was performed after use of bag failed to control bleeding.

Central placenta previa was treated by cesarean section, with five exceptions. Four of these patients, with still or previable fetuses, were treated by means of version or bag and version after perforating the placenta. The other patient with a breach presentation was treated with a bag placed extraovularly; a living child was obtained. In this case only a lip of the placenta covered the cervical os, the main portion lying in the lower uterine segment. In all five cases vaginal manipulation controlled the hemorrhage. The procedure of version and extraction should be kept in mind in treating the patient who has a central placenta previa associated with fetal death or previability, and with complete or almost complete dilatation of the cervix when the patient is first seen. Delivery may be accomplished and bleeding controlled in some of these cases more rapidly with this procedure than with section.

Abdominal delivery was used in 35, or 26 per cent, of the cases. In 22 of these cases there was a central placenta previa. Cesarean section was employed in approximately 81 per cent of the cases of complete placenta previa, and in

15 per cent of the incomplete varieties. Factors which influenced the decision to perform section in the thirteen cases of other types of placenta previa were age, parity, physical condition, hemorrhage, an unfavorable condition of the cervix, position and presentation of the fetus, questionably normal pelvis, and particularly important fetuses (such as in elderly primiparas). Cesarean section was employed twice after use of a bag had failed to control the bleeding. One section was employed because of hypertension, and a lowlying placenta was an incidental finding. The uterus was routinely packed with iodoform gauze after cesarean section.

Sixty-two, or 46 per cent, of the patients received other forms of treatment than abdominal delivery. In 28 patients, rupture of the membranes sufficed to control the bleeding. A Voorhees bag was used 17 times. Usually the largest bag that could be introduced through the cervix was chosen. It was inserted intraovularly 15 times, and extraovularly twice. Ten patients were treated by version and extraction, of whom two underwent a Braxton-Hicks version after perforation of the central placenta previa; in the other eight patients, the cervix was more than three-fourths dilated when the version was done. Extraction was never performed until complete dilatation of the cervix was attained. Five patients were treated with a bag and subsequent version and extraction. A Willett forceps was used once after use of a bag. This type of scalp traction is effective in the control of bleeding, and has been used more frequently in the past two years. Its use has been favored by certain authors,[14] but decried by others.[10]

The management of the third stage of labor after placenta previa is important, yet it is seldom stressed in the literature. When a patient has already experienced hemorrhage as a result of an obstetric complication during the first and second stages of labor, the obstetrician must be more alert and active in the treatment of third stage bleeding. Abnormal location of the placenta may lead to incomplete separation, and there may be bleeding from the trauma of delivery procedures.

In Table IV it is shown that 87 of the 134 patients had spontaneous deliveries of the placenta, and 35 underwent removal of the placenta according to the usual technique in a cesarean section. It was found necessary in 12 of the 99 cases of vaginal delivery to remove the placenta manually to control hemorrhage. Invasion of the uterus carries a well-recognized risk, but such risk is far less dangerous than continued blood loss.

TABLE IV. MANAGEMENT OF THE THIRD STAGE

MANAGEMENT	PLACENTA PREVIA, TYPE				TOTAL (134 CASES)	
	LOW-LYING	LATERAL	PARTIAL	CENTRAL	CASES	PER CENT
Spontaneous delivery	22	8	54	3	87	65
Manual removal			10	2	12	9*
Cesarean section	1	1	11	22	35	26
Uterine packs	2	3	17	3	25	19†
Postpartum hysterectomy			1		1	1

*Nine per cent of total cases or 12 per cent of vaginal deliveries.
†Nineteen per cent of total cases or 25 per cent of vaginal deliveries.

Hemorrhage continued after the placenta was delivered in 25 cases. In these instances, the uterine cavity was explored for retained fragments or possible rupture and was then packed with iodoform gauze. This procedure has fallen into some disrepute in recent years, but we continue to obtain excellent results by its employment when oxytocics and fundal compression fail to control

the bleeding. Barrett has stated that he packs the uterus routinely with iodoform gauze after either vaginal delivery or section in cases of placenta previa. In one of our patients, hemorrhage in the third stage was severe enough to necessitate hysterectomy. This operation should always be kept in mind as a possible lifesaving procedure in severe postpartum hemorrhage.[11]

Supportive Treatment.—The replacement of lost blood is the most important adjunct to the treatment of placenta previa. Table V summarizes the data on blood loss in our series. Over half of the patients had an estimated blood loss of less than 500 c.c. (grade 1). However, in placenta previa one cannot anticipate when minimal bleeding will suddenly become severe. It is our custom to "keep ahead" of the bleeding rather than to lag behind in the use of transfusion. Blood replacement before shock can develop is practiced. Continuous estimation of the amount of hemorrhage as it occurs is necessary as a guide to transfusion.

TABLE V. BLOOD LOSS

AMOUNT		PLACENTA PREVIA, TYPE				
GRADE	C.C.	LOWLYING	LATERAL	PARTIAL	CENTRAL	TOTAL
1	500 or less	21	4	36	12	73
2	501 to 1,000	0	3	29	8	40
3	1,001 to 1,500	2	2	8	7	19
4	1 501 or more	0	0	2	0	2

Each patient is given citrated blood of her own group and Rh factor from the hospital blood bank without awaiting cross matching. This has not resulted in an increase in transfusion reactions. However, cross matching is practiced when time permits.

If shock is present to the extent that veins are collapsed, transfusion is performed with positive pressure to hasten the replacement of lost blood. On occasion we have given the first 500 c.c. of blood in seven or eight minutes, and at times the blood is run into two separate veins simultaneously. The other usual supportive measures are employed. As soon as these measures are well under way, treatment directed at obstetric hemostasis is begun.

Chemotherapy should also be listed as an adjunct to the treatment of placenta previa. At the present time both chemical agents and antibiotics are administered prophylactically in cases in which there has been much vaginal manipulation. Unless there is a history of sensitivity to the drug, patients treated by cesarean section often receive 5 Gm. of sulfathiazole intraperitoneally. If complications develop in the postpartum period, chemical and antibiotic agents have an important position in treating them.

Results

Maternal.—Two mothers lost their lives as a result of placenta previa in this series. This gives an incidence of 1.5 per cent. A summary of these cases follows.

CASE 1.—The patient, aged 24 years, gravida ix, gave a history of repeated stillbirths. General examination, including special studies for syphilis, gave negative results. She had slight painless vaginal bleeding at the twenty-sixth week of pregnancy. She was admitted to the hospital on Aug. 3, 1925, at the twenty-eighth week of pregnancy, in labor and with profuse vaginal bleeding. Vaginal examination revealed that the placenta covered two-thirds of the cervical os. The membranes were ruptured and a version and extraction done; a stillborn infant weighing 1,814 Gm. was delivered. The placenta was removed manually. Immediately after this procedure the patient died suddenly on the delivery table. There were no notes in the records regarding transfusions or intravenous use of fluids. Autopsy revealed only ascites and hydrothorax. There was no rupture of the uterus.

In retrospect, it seems that if this patient had been investigated and treated at the time of her initial bleeding, she might have been saved. Also, when she was admitted with profuse bleeding, it appears that transfusion should have been started before vaginal examination was done.

CASE 2.—A patient, aged 43 years, gravida i, was admitted to the hospital on July 9, 1933, at the thirty-fourth week of pregnancy. She had had repeated episodes of slight painless vaginal bleeding since the twenty-sixth week of pregnancy. The fetus was in breech position, and a central placenta previa was diagnosed by rectal examination. No vaginal examinations were made. A classical cesarean section was done, with delivery of a living infant weighing 2,216 Gm. Central placenta previa was verified at operation. The mother had a stormy postoperative course, with a high fever, and died on the third postoperative day from paralytic ileus and peritonitis. Permission for autopsy was not obtained.

This case also demonstrates the danger of delay in treatment after initial symptoms have developed. It can be presumed that the repeated vaginal bleeding in this case was partially responsible for the subsequent infection. Whether modern-day chemotherapy and the administration of antibiotic agents would have altered the prognosis in this case is impossible to determine.

On the basis of the standard for morbidity of the American Committee on Maternal Welfare, in 27, or 20 per cent, of the cases morbidity occurred. In 17 cases morbidity followed cesarean section, and in 10 it followed vaginal delivery. Endometritis and parametritis did not occur in patients who underwent cesarean section. It is interesting to note that seven patients, or 5 per cent, had thrombophlebitis, the most common cause of morbidity in our series. Of these, two had nonfatal pulmonary emboli. Thrombophlebitis followed cesarean section four times and vaginal delivery three times. The incidence of thrombophlebitis was also high in the series of Davis and Campbell, and Ekas. The exact physiologic reason for this complication is not known, except for the increased incidence of thrombosis with any infection or anemia or both, and the lower location of big veins and sinusoids at the placental site. The other 20 patients had morbid conditions as follows: endometritis, four; parametritis, one; infection of the urinary tract, one; infection of the upper part of the respiratory tract, two; "caked" breasts, one; transfusion reaction, one; and undetermined conditions, ten. Very likely many of these ten represented mild instances of uterine infection.

Fetal.—Although most of the attention is directed toward the mother in cases of placenta previa, the outcome for the fetus is important. This is increasingly true, since the maternal mortality rates from placenta previa have approached zero.

The gross fetal mortality was 23 per cent, or 32 of 141 infants (Table VI). These statistics have not been corrected for prematurity, congenital anomalies, or intrauterine deaths, as in all these conditions the placenta previa itself may be wholly or in part the etiologic factor in the fetal loss. One must always regard "corrected" fetal mortality rates in placenta previa with caution.

Table VI shows an increasing number of surviving infants as weight increases. However, when fetal mortality is correlated with the type of treatment, few conclusions can be drawn. It would seem from Table VII that version and use of a bag offer a poorer prognosis to the fetus than section. However, the table also shows that one of the determining factors in electing the course of treatment was the condition of the fetus. The chances of the fetus were known in advance to be nearly hopeless in 17 instances. When one considers that 80 per cent of the patients with placenta previa are seen before term (Table II), it is surprising that the infant survival rate is as high as it is.

TABLE VI. FATE OF THE INFANTS

WEIGHT OF INFANT, GM.	TOTAL BIRTHS	STILL-BIRTHS	NEONATAL DEATHS	SURVIVALS	
				NUMBER	PER CENT
Below 1,000	3	2	1	0	0
1,000 to 2,500	57	12	9	36	63
2,500 or more	81	8	0	73	90
Total	141	22	10	109	77
Per cent of total births		16	7		
Gross fetal mortality, per cent		23			

TABLE VII. TYPE OF TREATMENT AND FETAL MORTALITY

TREATMENT, TYPE	TOTAL BIRTHS	INFANTS STILL OR PREVIABLE*	STILLBIRTHS	NEONATAL DEATHS
No treatment	39	7	1	6
Ruptured membranes	31	2	5	1
Voorhees bag	18	2	4	2
Version	10	4	7	
Bag and version	5	2	2	
Bag and Willett forceps	1			
Bag and breech extraction	1			
Cesarean section	36		3	1
Total	141	17	22	10

*Condition of infant at time treatment was started.

DeLee and Greenhill, and others have emphasized that fetal anomalies are numerous in pregnancies associated with placenta previa. In this series there were two infants who had anomalies incompatible with life, and five infants who had less serious anomalies. This gives a total of seven cases, or 5 per cent.

Discussion

There is fair agreement as to incidence, parity, classification, increased number of malpresentations, and other general factors in many of the papers on placenta previa in the past ten years. There is also agreement as to the risks of the condition and as to the importance of generous use of blood transfusion in treatment. However, there is difference of opinion as to its active management.

Johnson of Texas, Ekas of New York, and Macafee of England have pleaded for conservative management of this condition. These authors have stated that they do *not* think that it is always necessary to treat placenta previa at the time of the first hemorrhage, although they advise hospitalization. In the series herein reported, delay in treatment may have been a contributing factor in both maternal deaths. We feel that delay increases blood loss, the anemia, and the danger of infection. We justify delay only when the fetus in the particular case in question is of more than usual importance, such as in the case of a woman with a previous long period of infertility. Seeley, Schumann, and Adair have all pointed out the hazards of delay.

There is a fairly large group of obstetricians who favor dividing the treatment of placenta previa into two categories; namely (1) that of doing nothing or simply rupturing the membranes, and (2) that of doing a cesarean section. The advocates of this approach to treatment include Daichman and Pomerance,

Scott, Watson, Taylor, Barrett, and Cosgrove. In our series, the patients were treated by multiple methods, and the incidence of cesarean section was below the average reported in the literature.

From what has been said, it probably is evident that we do not consider cesarean section the routine treatment for hemorrhage from placenta previa. Often hemorrhage can be controlled by skillful vaginal manipulation; the "art of obstetrics" has a place in the management of the condition. Yet, there seems to be a trend at present to resort to cesarean section when confronted with almost any obstetric difficulty. DeLee* deplored this trend when he said that the tendency was to "cut" obstetric "knots" (by cesarean section) rather than patiently and skillfully to unravel them by the art and techniques of obstetrics. Admittedly, cesarean section usually is the easiest way out of difficulties for the attendant. In spite of the greatly enhanced maternal safety of cesarean section, it may be too optimistic to say that cesarean section is the best treatment for the condition or for the patient. The obstetric future of the patient as well as the immediate problem must be considered. The risk of repeated cesarean sections and the resulting limitation on the number of future pregnancies are factors which cannot be disregarded. As far as our own experience, herein related, reveals, our maternal and fetal mortality rates have not increased over the years, through which our attitude toward cesarean section for placenta previa has remained conservative.

In our series, treatment which was thought to fit was chosen in each case, taking into consideration the factors of age, parity, general physical condition, duration of pregnancy, estimated size of the fetus, amount of bleeding, the condition of the cervix, adequacy of the pelvis, position and presentation, and so forth. We have continued to employ the various vaginal procedures of use of a bag, version, Willett forceps, and often a pack in the uterus after delivery of the placenta. Blood has been given generously by transfusion. In recent years, antibiotics have been used both for prophylaxis and therapeusis. Thus, in this series we find a greater than average use of vaginal procedures and a less than average use of cesarean section (Table VIII). The maternal morbidity and mortality rates in this series justify the principles of treatment outlined above. In addition, the fetal salvage compares favorably with that of those who advocate the more liberal use of cesarean section. Matthews and Seeley also have advocated individualization of treatment.

In regard to maternal morbidity, thrombophlebitis seems to be the most important consideration. Infection predisposes to thrombosis, and reduction in morbidity from infection may be expected from the use of antibiotics. Anemia is another contributing factor to thrombosis. Barker and co-workers found an increased incidence of thrombosis and phlebitis in patients whose value for hemoglobin was below 12 Gm. per 100 c.c. of blood. It is probably best to administer blood by transfusion to obstetric patients undergoing hemorrhage, so that when they enter the puerperium the value for hemoglobin will be above 10 grams. But

*In order to represent this great deceased obstetrician fairly however, it should be noted that at the time of his death he favored relatively frequent use of cesarean section in placenta previa.

these factors have not entirely solved the problem of thrombosis. Various methods to combat thrombosis have been used extensively in surgical conditions with fairly good results. Perhaps some of these methods, notably the use of anticoagulants, should be given a more thorough trial in obstetric complications.

TABLE VIII. REPORTS FROM RECENT LITERATURE

AUTHOR AND YEARS COVERED	CASES	PLACENTA PREVIA, PER CENT	PER CENT			TYPE OF TREATMENT, PER CENT		
			MATERNAL MORTALITY	MATERNAL MORBIDITY	FETAL MORTALITY	NONE	VAGINAL	SECTION
Morgan 1937-1944	130	1.6	0		36	17.8	46.1	36.1
Ekas 1927-1943 (?)	86	0.6	2.3	40	55.8	41.8	53.6	4.6
Barrett 1938-1944	102	0.76	3.9					
Johnson 1939-1944	79	0.32	0		31.7	36.7	10.1	53.2
King and Chun 1936-1941	134	0.78	0.75		54			13.4
Ransom 1934-1943	215	0.8	0.93		22.3			
Seeley 1933-1942	250	0.78	2.8	31.2	34.6	23	53	24
Williamson and Greeley 1932-1944	162	0.4	3.1	58.4	31.1			47.5
Macafee 1937-1944	174		0.57		23.5	4	57	39
Scott 1928-1944	191	1.19	2.6		29.6			
Davis and Campbell 1931-1945	325	0.79	0.6	22.1	31.6	28.6	27.4	44
Daichman and Pomerance 1935-1946	165	0.43	0.6	41.2	25.8	12.7	27.8	59.3
Mayo Clinic 1918-1945	134	1.12	1.5*	20	23	28	46	26
Average		0.80	1.51	35.5	33.2	24	40.1	34.7

*One death occurred in 1925 and the other in 1933.

Summary

Placenta previa continues to be one of the more serious complications of pregnancy. A series of 134 cases occurring over a period of twenty-seven years is reported in this paper, with a maternal mortality rate of 1.5 per cent, a maternal morbidity rate of 20 per cent, and a gross fetal mortality rate of 23 per cent. The treatment in each case has been individualized according to the multiple factors present at the time of entry of the patient into the hospital. Although cesarean section has not been held in reserve, a greater than average number of patients have been treated by various vaginal manipulations without added fetal risk, and, to date, with maternal safety. The generous use of blood transfusion has contributed to the low morbidity and mortality rates. The complications of thrombosis and thrombophlebitis stand out as causes of maternal morbidity.

References

1. Aaberg, M. E.: AM. J. OBST. & GYNEC. **51**: 578, 1946.
2. Adair, F. L.: AM. J. OBST. & GYNEC. **49**: 94, 1945.
3. Barker, N. W., Nygaard, K. K., Walters, Waltman, and Priestley, J. T.: Proc. Staff Meet., Mayo Clin. **16**: 1, 1941.
4. Barrett, R. L.: Clinics **4**: 1055, 1945.
5. Cosgrove, S. A.: AM. J. OBST. & GYNEC. **50**: 404, 1945.
6. Daichman, Isidore, and Pomerance, William: AM. J. OBST. & GYNEC. **53**: 1024, 1947.
7. Davis, M. E., and Campbell, Alice: Surg., Gynec. & Obst. **83**: 777, 1946.
8. DeLee, J. B., and Greenhill, J. P.: Principles and Practice of Obstetrics, Philadelphia, 1947, W. B. Saunders Company.
9. Ekas, W. L.: New York State J. Med. **44**: 385, 1944.
10. Foreign letters: J. A. M. A. **113**: 1746, 1939.
11. Hunt, A. B.: AM. J. OBST. & GYNEC. **49**: 246, 1945.
12. Hunt, A. B., Mussey, R. D., and Faber, J. E.: New Orleans M. & S. J. **100**: 203, 1947.
13. Johnson, H. W.: AM. J. OBST. & GYNEC. **50**: 248, 1945.
14. King, Gordon and Chun, Daphne: Brit. M. J. **1**: 9, 1945.
15. Macafee, C. H. G.: J. Obst. & Gynaec. Brit. Emp. **52**: 313, 1945.
16. Matthews, H. B: AM. J. OBST. & GYNEC. **51**: 55, 1946.
17. Morgan, Joyce: J. Obst. & Gynaec. Brit. Emp. **51**: 509, 1944.
18. Persall, J. T., and Torpin, Richard: J. M. A. Georgia **33**: 297, 1944.
19. Ransom, E. M.: Journal-Lancet **65**: 212, 1945.
20. Schumann, E. A.: AM. J. OBST. & GYNEC. **49**: 93, 1945.
21. Scott, W. A.: AM. J. OBST. & GYNEC. **51**: 48, 1946.
22. Seeley, W. F.: AM. J. OBST. & GYNEC. **49**: 85, 1945.
23. Taylor, H. C.: AM. J. OBST. & GYNEC. **51**: 55, 1946.
24. Watson, B. P.: AM. J. OBST. & GYNEC. **51**: 53, 1946.
25. Williamson, H. C., and Greeley, A. V.: AM. J. OBST. & GYNEC. **50**: 398, 1945.

CERVICAL PREGNANCY

A Report of Two Cases and a Discussion of the Treatment

DANIEL G. MORTON, M.D., SAN FRANCISCO, CALIF.

(From the Division of Obstetrics and Gynecology, University of California Medical School)

CERVICAL pregnancy is a comparatively rare type of ectopic gestation which is of special interest because of the lack of knowledge regarding its etiology, the difficulties in making a correct diagnosis, and its high mortality. In the February, 1945, issue of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, Studdiford published a fairly comprehensive review of the literature; he found 14 certain cases, 14 probable cases, and added two probable cases of his own. The *Index Medicus* lists a few references (case reports) in addition to those quoted by Studdiford, and at least two cases have been reported since his review, one by Bowles and one by Fearl. Numbers of others must go unrecognized or unreported. Within the last several years I have encountered two cases, one a "probable" case and the other one a proved case, because surgical intervention was demanded and provided us with the pathologic proof. Studdiford's article contained an excellent review of the symptoms, signs, and basic pathology of the condition. I wish to report my two cases in order to underline the potential dangers of cervical pregnancy, because one of the cases is such a good pathologic demonstration of the condition, and because of the therapeutic considerations which these cases brought up.

CASE 1.—J. M., No. 118199, aged 26 years, para i. The patient was first seen because of sterility of ten months' duration. She had had one normal spontaneous delivery at term three years previously. Her past history was entirely irrelevant. Menses began at 11 years of age, and came every 26 days for five days. Examination revealed a slim, healthy-appearing young woman. She was entirely feminine and presented no evidences of glandular imbalance. Heart and lungs were negative. The abdomen was negative. The pelvic organs were entirely normal except for deviation of the uterus to the left, perhaps due to a small scar in the left fornix, continuous with an old cervical laceration. The patient was advised to temporize. Six months later, on June 28, 1945, the patient had what she interpreted as a normal menstrual period. About one month later, on July 24, she began to have spotting from the vagina which continued for five days, then stopped. After another week, frank bleeding began and continued daily for four weeks. There were no cramps. Other signs of pregnancy were present, such as breast fullness and slight nausea. She was not examined at this time. It was assumed that the patient was aborting. Ergotrate produced neither more nor less bleeding. A few days later the patient passed a number of clots and some tissue, she thought. Bleeding ceased for two weeks, at which time a vaginal examination was made. The external os was found to be dilated 2 cm. and obliterated. Lying in the cervical canal was a mass of placental tissue. The uterine body seemed about normal in size and retracted above the cervix proper. My impression was that this represented the cervical stage of an abortion. I thought that the uterus had expelled its contents into the cervix, which had ballooned out to accommodate them. The

patient was advised to enter the hospital for the completion of the abortion. This she did on Sept. 11, 1945. Her hemoglobin at this time was 87 per cent (12.9 Gm.), blood pressure 120/55. Under Pentothal anesthesia the cervix was exposed and the placental tissue was grasped with an ovum forceps for removal. Some of it came away easily, but a considerable amount of tissue could be removed only by pulling it forcibly. This resulted in profuse bleeding, the origin of which appeared to be the posterior wall of the dilated cervix. Digital palpation of the interior of the cervix revealed a cavity about 3 to 4 cm. in diameter, a very soft, thin, and ragged posterior wall, the internal os at the top of this cavity, no bigger than lead-pencil size. It was at this time that a diagnosis of cervical pregnancy was made. The cervical cavity and the vagina were tightly packed with gauze and the patient was returned to her room. The packing was removed the next day, but resulted in so much bleeding that it was necessary to repack immmediately. A 500 c.c. transfusion was given at this time. On the following day, Sept. 14, 1945, the hemoglobin had dropped to 70 per cent (10.1 Gm.). A second attempt was made to remove the packing very gradually. The patient did not bleed very much at first, but by the next day was soaking pad after pad and looked very pale. Hemoglobin at this time was 66 per cent (9.7 Gm.). The cervix was exposed and incised transversely with the idea of clamping or suturing the bleeding area directly. This was not very satisfactory. Finally the canal was packed with fibrin foam and transfixed with a figure-of-eight suture. Bleeding ceased. No gauze packs were inserted. The patient received two transfusions of 500 c.c. each that day, and another one two days later. A week passed with only vaginal spotting, then profuse bleeding started again and required repacking with fibrin foam and gauze. It was then decided to take the patient to surgery the next day, and if definite and satisfactory hemostasis could not be achieved vaginally, hysterectomy was to be resorted to. The patient was transfused with 500 c.c. of whole blood. The cervix was exposed; very little bleeding occurred. There had been definite shrinkage of the organ and undoubted thrombosis of vessels. My efforts were confined to approximation of the lateral incisions which had been made at the previous operation. The restoration of the cervix and effective hemostasis were thus accomplished. The patient received her sixth and seventh transfusions during the next few days. No further bleeding occurred, and the patient was discharged from the hospital in good condition ten days later. Two days before discharge her hemoglobin was 82 per cent (11.9 Gm.). Subsequently the patient became pregnant again and delivered spontaneously at term without difficulty.

Though there appears to be little doubt of the correctness of the diagnosis, this case must be labeled as "probable," since we have no absolute proof. Fortunately, the pregnancy terminated at an early stage, and fortunately, too, it was possible finally to achieve hemostasis without resorting to hysterectomy. It followed the pattern described by Studdiford for other cases in which there was an early termination of the pregnancy. In the majority of these instances it has been possible to control the bleeding without hysterectomy, although, in many hemorrhage of alarming proportions has occurred before the final control. Tight packing of the area, probably of much longer duration than was allowed in the case reported, would seem to be of great importance.

Case 2.—V. B. The patient was a 28-year-old white, separated, office worker, gravida ii, para 0, who first entered the San Francisco Hospital on Sept. 12, 1946, with a chief complaint of cramps and vaginal bleeding of one day's duration. The patient's last regular menstrual period had occurred on May 23, 1946, and was normal in duration and amount. She had had morning nausea and breast tenderness during the three months prior to entry to the hospital. Otherwise, the course of her early pregnancy had been uneventful. On Sept. 10, 1946, the patient had a sudden gush of blood from the vagina and experienced abdominal cramps.

On her admission to the hospital, the temperature was 102° F. orally, pulse 110, blood pressure 120/70. She appeared in good general condition without evidence of shock. Examination of the abdomen revealed generalized tenderness especially over the lower quadrants. No

masses were palpable. Speculum examination revealed a large bluish cervix. The os was not dilated, and there was a small amount of blood in the vaginal canal. No placental tissue was visible. A tentative diagnosis of incomplete or threatened abortion with endometritis and pelvic peritonitis was made. Cervical cultures were taken and showed hemolytic streptococci. Laboratory examination revealed: hemoglobin 70 per cent; white blood cells 9,250, and normal urine. Wassermann was negative. The patient was given penicillin and bed rest. She remained in the hospital for ten days during which time she received a transfusion of 500 c.c. of whole blood. Temperature was normal after the third hospital day. Only a minimal amount of bleeding occurred.

Twenty-four days later, on Oct. 15, 1946, the patient was readmitted to the hospital with the following story: After leaving the hospital she remained asymptomatic until one week prior to readmission, at which time she developed more vaginal bleeding and abdominal pains. This continued intermittently. For the last twenty-four hours she had passed large clots and felt feverish. Examination revealed the patient to be slightly pale, talkative, and quite apprehensive; temperature 103.2° F. orally, pulse 132, blood pressure 120/70. Laboratory examination: hemoglobin, 65 per cent; 1 plus acetone in urine. Speculum examination showed a moderate degree of cervical dilatation. Protruding from the external os there apppeared to be products of conception. These were gently removed by means of sponge forceps, and found to consist of a macerated fetus (length, 32 cm.). Immediately thereafter there was a profuse hemorrhage which could not be controlled by uterine massage and parenteral Ergotrate (both intramuscular and intravenous). The lacerated umbilical cord broke, and no attempt was made to remove the placenta, as the patient was rapidly going into shock. Immediately the vagina was packed and 2 units of plasma were given intravenously; within the next 45 minutes 1,500 c.c. of whole blood were administered. Gradually the patient responded and by morning the blood pressure had risen to 92/60 and the pulse had stabilized at 120. There was no bleeding through the pack.

It was deemed advisable to remove the uterine pack the following morning, and if no bleeding recurred an attempt was to be made to remove the placenta. Under cyclopropane anesthesia the pack was removed. Since there was no immediate bleeding, 2 fingers were introduced into the patent cervix, where the lower edge of the placenta could be felt. On manipulating the placenta so much bleeding occurred that no further attempt was made to remove it. Five minims of Pitocin in 20 c.c. of saline were given intravenously and the fundus massaged; however, profuse bleeding persisted. The uterus was then packed tightly with gauze. Total blood loss at this time was measured at 2,600 c.c. The patient was in profound shock again and a transfusion was started immediately. She received four transfusions within the next twelve hours.

On October 17 (i.e., 24 hours later) a second attempt was made to remove the uterine pack very gradually. Before this could be completed profuse bleeding recurred, measuring 1,900 c.c. The uterus and vagina were repacked and three transfusions were given. The correct diagnosis had not been made at this time; however, it seemed obvious that the bleeding could not be controlled vaginally and that a hysterectomy would have to be attempted. Within five hours of the last episode of bleeding the patient's blood pressure had risen to 90/60, and her pulse rate was 126. It was thought that her condition was good enough to permit laparotomy. Under cyclopropane anesthesia the abdomen was opened, with the following findings: The uterine body itself was only slightly enlarged and was perched on top of a large distended mass which was interpreted as the lower uterine segment markedly distended with packing and placental tissue. This distended mass was at least 9 cm. in diameter. Its anterior wall was soft, seemed rather thin, and contained many large distended veins. The uterine pack was slowly withdrawn from below in order to reduce the volume of the mass and permit an approach to the vessels. Dissection was carried down on either side of the uterus to the level of the uterine arteries. The cervix of the uterus could not be identified as such and it now became apparent that it was incorporated in the large soft mass. It was

not until this time that the diagnosis of cervical pregnancy was made. Although not much bleeding had occurred upon removal of the pack, it was not possible to carry the dissection low enough to remove the entire cervix because of the volume of the mass which almost completely filled the pelvis. It was necessary to amputate the uterus at an undetermined point in the cervix as low as could be reached. In cutting across it, placental tissue was also incised. Fortunately, the sutures closing the friable cervical walls sufficed to control immediate hemorrhage. It was hoped that the remaining placental tissue would separate and be expelled spontaneously.

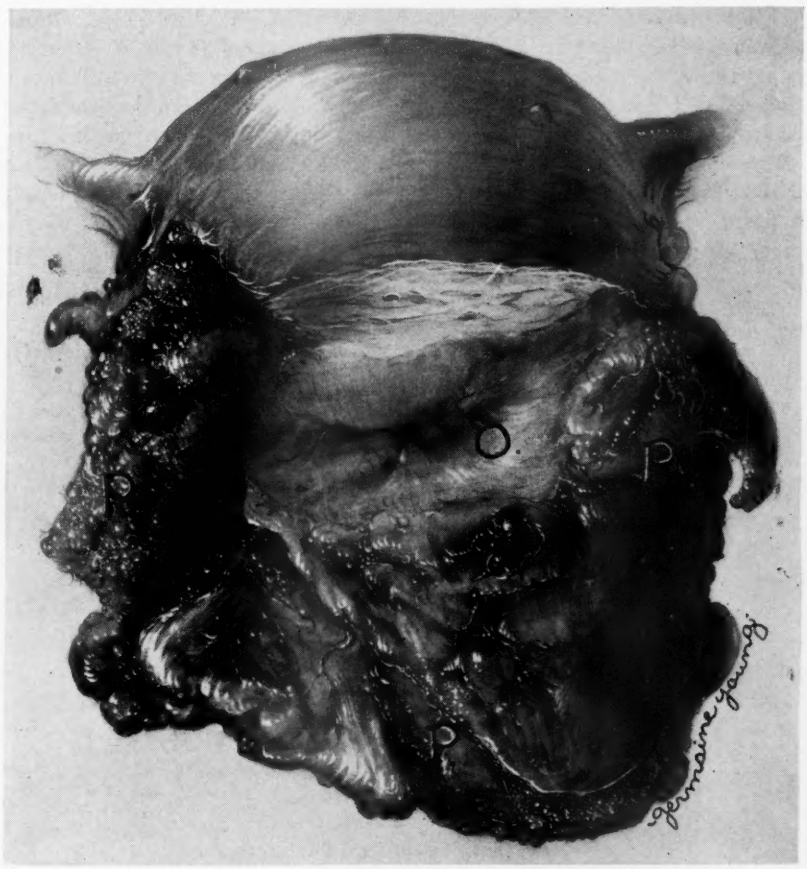


Fig. 1.—Posterior view of the amputated uterus. The internal os (O) is clearly visible. Placental tissue (P) attached to the greatly elongated and thinned out cervix comes to within 1½ to 2 cm. of the os.

The postoperative course was morbid up to the fourth postoperative day, when the temperature fell to normal. Patient received an additional 2,500 c.c. of blood on the day of her laparotomy, 200 c.c. the following day, and an additional 1,000 c.c. on the third postoperative day. By the fifth postoperative day the hemoglobin was 9.4 Gm. An additional transfusion was given on the sixth postoperative day and the hemoglobin rose to 10.8 Gm. On the ninth postoperative day a small amount of vaginal bleeding recurred. A small pack was placed in the remaining portion of the cervix and removed after twenty-four hours with minimal bleeding. On the fifteenth postoperative day more bleeding occurred; an Oxycel pack was placed in the cervix and seemed to control the bleeding. The patient was given additional blood during this period. A moderate amount of vaginal bleeding persisted intermittently. Vaginal examination on the thirty-fourth postoperative day revealed the cervix to be soft

and intact except for a small rent in the posterior wall at the external os. In the region immediately above and anterior to the cervical os there was a large, round, firm mass some 8 cm. in diameter which was thought to be the remains of the cervical body distended by the placental tissue which had not been removed at surgery. Because the patient had passed no placental tissue since surgery and the external os was now very small and bleeding was continuing, it seemed advisable to attempt removal of the remaining cervical stump with its contents.

Consequently, on November 22, the patient was taken to surgery again. A second laparotomy was performed, and at this time it was found that the cervical stump was still very large, being distended and filled by large pieces of old placental tissue. Because of the inflammatory induration about the cervix and the intimate adhesion of the overlying bladder anteriorly and the bowel posteriorly, it was deemed advisable simply to evacuate the cervix and close it without further operative procedure. The cervix was opened at its superior aspect and the placental tissue removed by sponge stick until the entire cavity appeared free of visible placenta. The top of the stump was resutured and the abdomen closed. The patient made an uneventful recovery without further bleeding. She was discharged from the hospital on her fourteenth postoperative day after the second laparotomy, or a total of 53 days after the initial surgery. During her hospital stay the patient received 11,000 c.c. of whole blood.

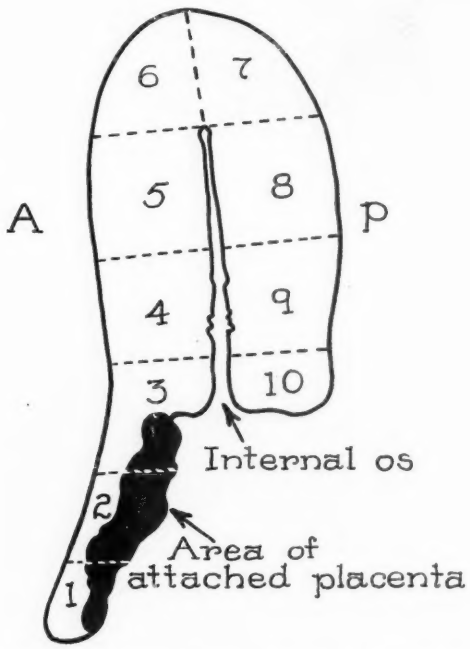


Fig. 2.—Blocks were cut from a 3 mm. thick slice of tissue taken from the sagittal plane as indicated in this diagram. Confirmatory blocks were also cut in adjacent planes.

Pathologic Report.—The specimen consists of the enlarged, intact uterine body which has been amputated through its posterior wall just below the level of the internal os. In other words, the anterior wall of the corpus is continuous inferiorly with a flaplike projection of tissue extending down from the region of the internal os, presumably the thinned out cervical wall. Only the outer 3 mm. of this projection is composed of the usual fibromuscular layers; the remainder of its thickness varies from 0.5 to 1.0 cm. and is composed of dark friable tissue resembling placental tissue. The latter tissue reaches to within 1.5 cm. of the internal os superiorly, and appears to have been cut off with the cervical wall, which does not include the external os inferiorly. The drawing and the diagram illustrate these findings perfectly.

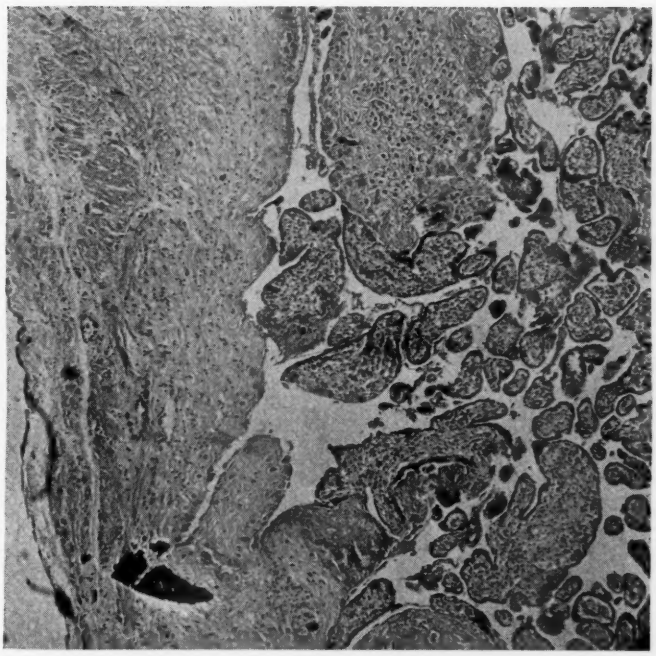


Fig. 3.—Section from block No. 1 as indicated in Fig. 2. The thinness of the cervical wall is well illustrated. No cervical glands are seen.

Fig. 4.—Section from block No. 3 as indicated in Fig. 2. This is the uppermost margin of the placental site, and it lies below the internal os.

A sagittal section of tissue was removed from the midline area and cut into blocks, as indicated in Fig. 2, so that a microscopic survey of the entire uterus could be made in this plane. The sections revealed that the corpus was lined by a thin layer of endometrium exhibiting little or no decidual response, but showing some diffuse inflammatory reaction, most marked near the internal os. There were no evidences of placental fragments, neither villi nor chorionic cells, in the body of the uterus. Sections from the flap of tissue below the internal os showed placental tissue, both well preserved and degenerated, beginning at the point on the anterior cervical wall 1.5 cm. below the internal os, extending down to the cut margin, and implanted on a very thin layer of fibromuscular tissue. There was no definite decidua between placenta and cervical wall. Cervical glands could not be identified in the sections taken. Numerous large blood sinuses underlay the placenta, and there was a spotty inflammatory reaction near the areas of partial placental separation. *Diagnosis:* Cervical pregnancy with partial separation.

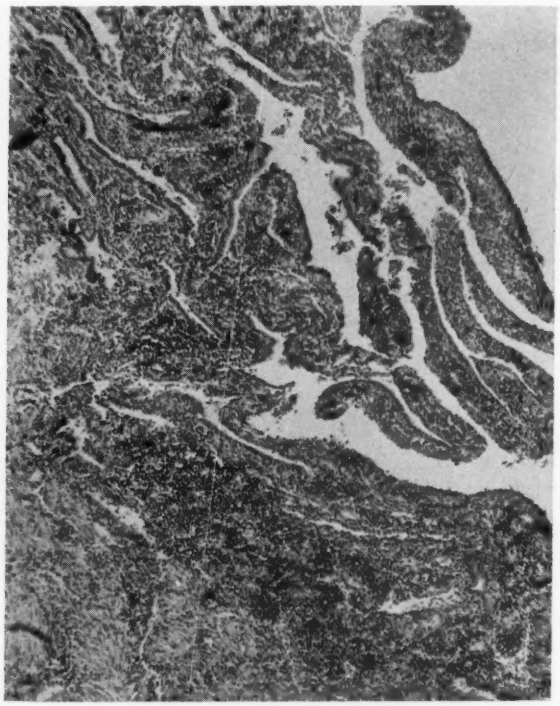


Fig. 5.—Section from block No. 4 as indicated in Fig. 2. A considerable leucocytic infiltration is present. No frank decidual reaction is visible.

Comment

Fortunately, cervical pregnancy is rare, because it is an extremely dangerous condition—there was a 20 per cent mortality in Studdiford's cases. Much of the danger arises from the fact that it is difficult to make a diagnosis before procedures have been instituted which may result in massive hemorrhage; i.e., specifically, attempts to remove the placenta. The frequency of abortion, with which it is usually confused, and the rarity of cervical pregnancy combine to dull one's diagnostic acuity. If one should happen to have an opportunity to examine the patient before some separation of the placenta and bleeding had occurred, ballooning out of the cervix above a flattened-out cervical canal and external os would constitute the significant findings. If the pregnancy should have progressed beyond the first three or four weeks, the

body of the uterus might possibly be palpable above the ballooned-out cervix, simulating a fibroid at the fundus, of the "monkey-cap" variety. If, as is usually the case, some bleeding has already set in, then of course the similarity to threatened or incomplete abortion is great. It appears that the products of conception are not expelled with as much dispatch as in the usual abortion, however. This is readily understood when we reflect that the force of uterine contractions is absent; we have to deal with the relatively passive and scanty cervical musculature. Thus, undue delay in the completion of abortion should put us on guard. At this point, conditions may now prevail which may very much suggest the cervical stage of an abortion; it may well appear that the uterus has expelled its contents into the cervix which has gradually become ballooned out to accommodate them—and there they have been retained, with perhaps slight or moderate intermittent serous discharge and bleeding. Forceful removal of even a small portion of the placenta in the early stages of the process usually results in copious hemorrhage. This undesirable result is easily comprehended when it is realized that there is no muscular mechanism in the cervix designed to clamp off the subplacental blood sinuses at separation, as there is in the corpus. Naturally, the more advanced the pregnancy, the more copious the bleeding is likely to be.

Every effort should be made to make the diagnosis before any manipulation is undertaken. Separation of the placenta should be avoided, and indeed the placenta might profitably be tightly packed against the cervical wall, particularly if there has been a partial separation. Thrombosis of vessels and gradual absorption should occur in just the same manner as they do with a placenta left in the peritoneal cavity after an abdominal pregnancy. The placenta implanted in the cervix should not be disturbed any more than should the placenta implanted upon bowel and its mesentery. Finally, at removal, preparations for immediate transfusion and repacking should be at hand, since exsanguination may occur in a very short period of time. It is possible that in time the placental tissues would be absorbed completely.

As a number of the reported cases indicate, bleeding may be so difficult to control that hysterectomy is demanded. Often this is unfortunate because of the youth of the patient; it can probably be avoided in the majority of the early cases. With more advanced pregnancies there is far more likelihood that hysterectomy will be demanded eventually.

Obviously, the ability to manage cases of this kind successfully, particularly when recognition has been delayed and hemorrhage has been great, depends upon the availability of blood in large amounts, and an alert hospital staff.

It is hoped that the report of these cases and the airing of the views I have acquired from my experiences with them will assist in making some others alert to this very trying condition, and will help to guide them should they encounter such a case.

UTERINE DYSTOCIA*

M. Pierce Rucker, M.D., Richmond, Va.

THERE is no need of defining dystocia to a group of obstetricians and general practitioners. We all have had enough experience with painful or slow labors to understand what the term means. Mechanical dystocia, due to cephalopelvic disproportion, malpositions, short cord, etc., has always overshadowed other forms of dystocia in our thinking and teaching, probably because a contracted pelvis or an oversize baby is easy to recognize and the mechanics of such obstruction is easy to understand. This type of dystocia is becoming relatively less important for the reason that marked pelvic deformities are rapidly disappearing. This is especially true in private practice, but even in the clinic population, nutrition has improved so greatly that a rachitic pelvis has become a rarity. Our thanks are due to the public schools for this great improvement. For instance, a survey of the school children in Richmond several years ago showed a smaller percentage of undernourishment among the Negro children than among the whites. The schools that showed the most undernourishment were in the so-called best neighborhoods. The explanation that was advanced was that the poor children did what the teacher told them to do but the rich children and their parents knew better.

I wish to discuss at this time dystocia caused by dysfunction of the uterus. The slow, difficult deliveries due to faulty uterine contractions have long been recognized.

Paulus Aegineta[1] (626-690) in the seventh century taught that "difficult labour arises either from the woman who bears the child, or from the child itself, or from the secundines, or from external circumstances. From the woman in labour, either because she is gross and fat, or because her whole womb is small, or because she has no pains, or is affected with fear, or because the uterus or some other part is inflamed or otherwise diseased, or because, from some natural weakness, she is unable to expel the foetus, or because the labour is premature." Smellie[2] clearly understood that various parts of the uterus could contract irregularly. Dewees[3] called this condition partial contractions of the uterus. Other terms that have been used are strictures of the uterus[4] and irregular or spasmodic action.[5] Recently, Jeffcoate[6] described these conditions under the term "incoordinate uterine action." It seems to me that uterine dystocia is a better term. It includes several related conditions to which various names have been attached: inertia, uterine dyskinesia, dystocia dystrophia, hourglass contraction, and constriction ring.

I became interested in constriction rings in 1924[7] when Dr. James Garber of Birmingham, in commenting on my paper, "The Action of Adrenalin on the Pregnant Human Uterus," said that the drug ought to be good for contraction ring. I have confined my talking and writing to constriction ring dystocia, because it was a definite condition that I could feel and be certain

*Read before the Alabama Association of Obstetricians and Gynecologists, April 14, 1948.

about. I have never implied that it is the only type of dysfunction of the uterus. Today most obstetricians will agree that it is the most exaggerated form, just as eclampsia is the worst form of the toxemias of pregnancy. We know that many of these rings are reversible, and will disappear in time, although some will persist even after death. We know that they may occur in the third stage of labor, when we speak of them as hourglass contractions, and we have reason to believe that they may occur early in the first stage of labor, before the cervix is sufficiently dilated to permit an exploration of the interior of the uterus, and so definitely diagnose a ring. In such an event, the differentiation between constriction ring and inertia is extremely difficult, or even impossible.

Similarly, a rigid cervix is something that can be felt. It may persist for hours and may seem to be the sole reason why the baby is not born, and yet when the uterus begins to contract in an orderly manner the rigidity disappears. I had a dramatic example of this a number of years ago. The patient was a 39-year-old multipara whom I saw in consultation. Several years previously, a general surgeon had amputated a portion of her cervix. When I saw her she was 36 weeks pregnant, her membranes had ruptured, and she had been having indifferent labor pains for over twenty-four hours. She had had a chill and her temperature had risen to 103 degrees. The cervix was rigid and undilated. Her doctor was at a loss as to what to do. I advised him to give her ¼ grain of morphine and $\frac{1}{200}$ grain of hyoscine, and go home and go to sleep, and not to blame the nurse if the patient delivered the baby in bed. Sure enough that is just what happened. About 2:00 A.M. the patient awoke, had two pains, and the baby was born before even the intern could get to her. I can recall only two cases where the rigid cervix would not dilate and where I felt that Dührssen's incisions were indicated. Those who consider cervical dystocia a distinct entity define it as difficult labor due principally to failure of the cervix to dilate and be effaced within a reasonable time despite frequent and forceful uterine contractions. Such a definition well describes many cases of constriction ring dystocia and it is quite possible that many cases would be considered constriction ring dystocia by one clinician and cervical dystocia by another. Sackett[8] found cervical dystocia in 1.05 per cent of 8,213 confinements at the Woman's Hospital. It was the major cause of 13.4 per cent of 382 prolonged labors and the major indication for 9.5 per cent of 474 cesarean sections. Almost 6 per cent of the high forceps, 3.6 per cent of the midforceps, and 1.7 per cent of the low forceps operations were due to this syndrome.

Colicky pains, uterine inertia or atony, and uterine dyskinesia are less definite, or possibly I should say they have no definite physical signs. They may occur independently or they may alternate in the course of a single labor. Jeffcoate aptly says that the conditions have the same etiologic factors (primiparity, nervousness, posterior positions, etc.) and they require treatment on similar lines. For that reason he includes inertia among the incoordinate uterine actions.

Finally, a word about dystocia dystrophy. This pituitary disturbance produces definite signs. These heavy-set, short-fingered women are prone to have uteri that do not function well, but this is not invariably so. It should be considered a predisposing cause of uterine dystocia and not a form of that condition.

One is apt to assume that the efficiency of uterine contractions in labor depends upon their strength and duration, which in turn parallels the amount of pain felt. This, however, is far from the actual fact. Some twenty-five or more

years ago, when I recorded on a kymograph variations in intrauterine pressure every time I used a Voorhees' bag, I noticed frequently that small contractions of 5 or 10 mm. Hg pressure would dilate the cervix rapidly in some cases, whereas, in other cases, particularly in premature cases, strong contractions of 40 to 50 mm. of Hg had little or no effect on the cervix. More recently, the group at the University of Georgia[9] has studied this more carefully. By introducing balloons at various levels in the cavity of the uterus they have shown that both the pregnant and nonpregnant human uterus may contract in an orderly or in a disorderly manner. They have actually demonstrated a constriction ring in a nonpregnant uterus. If the contractions are coordinated, the contents of the uterus, be it fetus, ovum, or blood clot, are expelled, but if the contractions are uncoordinated the uterine contents remain stationary. On Jan. 30, 1948, at a Conference on Normal and Pathological Physiology of Pregnancy, S. R. M. Reynolds[10] reported his work with external hysterography using a differential tocodynamometer. He also showed that the pregnant human uterus acted in various ways. It was only when the contractions of the fundus were stronger and longer than those of the midportion, and those of the midportion were stronger and longer than those of the isthmus, and those in turn stronger and longer than those of the cervix, that progress of labor was made.

Thus we have evidence obtained by laboratory methods that the uterus can and does act incoordinately and ineffectually. We have known this clinically for years, but it is nice to have scientific support for our clinical beliefs. Uterine dystocia may take various forms as already indicated and these forms are not necessarily fixed and constant. It may occur when there is no mechanical cause for a long and difficult labor or it may occur when the patient has some disproportion between the fetus and the pelvis. In other words, there are cases of purely uterine dystocia and cases of purely mechanical dystocia, and there are cases in which there is some disproportion and some uterine incoordination. When there is this overlapping of the two conditions, there is opportunity for the display of nice clinical judgment.

The effect on the course of labor is well described by Jeffcoate. Since my studies have been chiefly with the severer type, i.e., constriction ring dystocia, I quote from him lest someone might think my picture too pessimistic. Incoordinate uterine action, he says, "even to the extent of constriction ring formation, can occur during any stage of labor, before or after rupture of the membranes. In the third stage, the typical example is 'hourglass contraction' of the uterus. The general effect of incoordinate uterine action is to prolong the course of labour, especially the first stage. The cervix dilates slowly but after a distressing and long first stage may become fully dilated. In the common but less serious cases, and especially if the fetal head rotates favourably, the second stage may be normal and delivery spontaneous. If the disturbance of function is more severe, the woman is exhausted or the fetus is showing signs of distress by the time the second stage is reached and forceps delivery becomes necessary. This may be difficult, especially if a constriction ring persists or forms during the second stage. Quite frequently the cervix never really attains full dilatation and a 'rim' has to be slipped up over the presenting part before the forceps blades are applied. In the most serious cases the cervix may be only half dilated or less, even after several days of labour."

The etiology of this condition is obscure. Various causes have been advanced—bags, bougies, rupture of the membranes, oxytocics, malpositions, fear and anxiety on the part of the mother, etc. In 1946[11] I analyzed my

cases of constriction ring, which at that time amounted to 202. There were 102 cases in 7,354 induced labors, or 1.38 per cent, and 100 cases in 6,221 uninduced labors, or 1.6 per cent. When labor was induced by amniotomy, a constriction ring formed in 1.46 per cent of the cases, and when labor was induced by bags, a ring formed in 1.25 per cent. In 748 cases, small doses of Pituitrin were used before labor started or in the early part of the first stage and in these a constriction ring formed in 2.8 per cent of the cases. In 483 cases, the membranes ruptured spontaneously before labor began, and in these there was a constriction ring in 2.7 per cent. The average age of the patients who developed constriction rings was 28½ years which was more than two years greater than the average for the whole series of 13,575 cases. Only 30 had occiput anterior positions and more than one-half of the patients had a borderline contraction of the pelvis. In other words, these patients were slightly substandard obstetric risks. I have a feeling that the condition is a fatigue phenomenon. Such a theory certainly furnishes a good guide to the treatment.

Prognosis

The earlier writers reported high maternal and fetal mortality. The chief dangers to the mother are exhaustion, shock, postpartum hemorrhage, and infection, on the one hand, and injuries to the uterus, cervix, and vagina from attempts at delivery, on the other hand. The fetus may die from asphyxia, birth trauma, intrauterine pressure, or intrauterine infection. Dr. Edwin Rucker recently had an instructive case in this connection. It was a consultation case and an x-ray examination was done to rule out disproportion. The plate showed overlapping of the fetal skull bones which subtended arcs of different circles. The roentgenologists made a diagnosis of a dead fetus. The fetal heart tones were not heard. The patient was anesthetized and examination with the whole hand showed a constriction ring. The ring was relaxed with Adrenalin and the baby was delivered by version and extraction. He was easily resuscitated and left the hospital with his mother in good condition.

Rudolph[12] in his last report had a fetal mortality of 32 per cent and a maternal mortality of 3.5 per cent. In a former report[13] he stated that the fetal mortality should be reduced to less than 15 per cent. Herman Johnson,[14] whose idea in dealing with this condition is early diagnosis and prompt delivery, lost no mothers and had a fetal mortality of only 5 per cent in 105 private cases. My only fatal case occurred in my first twenty cases, before I had learned the value of Adrenalin. The patient was a Negro woman, the mother of 13 children, who was admitted to St. Philip Hospital after failed forceps and version elsewhere. The ring did not relax under deep chloroform anesthesia, and the fetus, which was macerated, was delivered by craniotomy. The mother did not recover from the anesthesia. In 1947,[15] I reported my fetal results in detail. At that time I had had 216 cases with one set of twins. There was a gross fetal mortality of 19.3 per cent. In the last 150 cases the fetal mortality was 12 per cent. Since that report was written (1946) there have been 2,698 deliveries at the Johnston-Willis Hospital and deliveries at other hospitals conducted by Dr. Edwin Rucker, Dr. Hudson, or me, and in this number there were 54 with constriction rings. A ring was felt in each case. None was delivered by cesarean section. All 54 mothers and 54 babies survived. In view of our recent experience and now that penicillin is available for patients whose membranes have been ruptured for a long time, I feel that the prognosis is a great deal better, even in the worst cases. If one keeps up the fluid intake and the electrolytic balance and uses

good judgment both as to when and how the patient should be delivered, there is no reason for losing either mother or baby. The worst feature from the mother's standpoint is the time wasted while the cervix is dilating.

Treatment

The first essential in treatment of these tedious labors is to guard against the mother's becoming dehydrated and exhausted. She should be encouraged to drink liquids and eat simple food. Fruit juices are particularly valuable. If she does not take sufficient fluid by mouth, she should be given glucose solution intravenously or by rectum. Small doses of morphine are invaluable early in the first stage of labor. We have found magnesium sulfate (20 c.c. of a 10 per cent solution) given intravenously also helpful. After a rest, the "pains" are apt to become orderly and effective. In cases of pure inertia, Eastman[16] and Reid[17] advocate very small doses of Pituitrin repeated at 30 to 45-minute intervals until contractions become effectual. This treatment is recommended only in cases of primary inertia, a diagnosis that is sometimes hard to make. In a five-year period, there were 463 such patients at Johns Hopkins and in the same period there were 1,609 such patients at Harvard. In both clinics there was a great reduction in midforceps operations.

If the membranes have been ruptured for twenty-four hours, I have been in the habit of starting the patient on penicillin and continuing its administration until delivery. If the fetal membranes are opaque, indicating an amniotic sac infection, the penicillin is kept up for another twenty-four hours.

When the cervix is fully dilated or almost fully dilated, I am convinced that it is best for both the mother and child to effect a delivery. The patient is anesthetized and the whole hand is introduced into the uterus to determine if there be a constriction ring present. If a ring be found, it can usually be relaxed with 5 or 6 minims of Adrenalin hypodermically. The ring can be felt to relax in a few minutes, but sometimes it takes as long as a half-hour. Occasionally Adrenalin fails. In that case amyl nitrite might be tried. Recently I had a case in point.

The patient was a 30-year-old primipara, a former nurse, who consulted me on Feb. 17, 1947. At that time, her physical examination was normal. She gave a history of dysmenorrhea. She was due by Nägele's rule on September 29. In March, her blood pressure had risen to 140/80 and it remained elevated the remainder of her pregnancy in spite of a salt-poor diet. On September 6 it was 160/80 and she had a little albumin in her urine and slight edema of the ankles. On September 13, the blood pressure was 150/80 and the patient was nervous and irritable. Termination of pregnancy was advised. On September 24, the cervix was partly effaced and admitted 1½ fingers. Labor was induced by aminotomy. The patient began to have labor pains in seven and one-half hours. In two and three-quarters hours more, the cervix was completely dilated and the head was on the perineum, and in a right occipitotransverse position. Vaginal examination showed that there was still a rim of cervix encircling the head like a loose hat band. An attempt was made to apply Kielland forceps but was unsuccessful on account of a constriction ring. One-half c.c. of Adrenalin was given hypodermically but had no effect on the ring. A large wheal formed at the site of injection which may have been the reason that the uterus was unaffected. The dose was repeated one-half hour later with the same results. Most of this time the patient was under ether anesthesia. Her pulse was now 190 per minute. An ampule of amyl nitrate was broken in the ether mask and the anesthesia continued. The ring disappeared within two minutes. The forceps were applied without difficulty and an easy extraction was done. Just as I remarked, "There goes the ring," the anesthetist noticed that the patient's pulse had dropped to 90 per minute. The baby, a girl, breathed at once. She weighed 5 pounds, 13¾ ounces and

measured 20⅝ inches. Both mother and baby made an uneventful recovery and left the hospital on the seventh day.

When the constriction ring relaxes, the patient should be delivered either by version and extraction or by forceps. The Kielland or the Luikart modification of Kielland's forceps is especially useful in this type of delivery. In other types of uterine dystocia, of course, there is no need of the Adrenalin or the amyl nitrite. Should you apply forceps without previously determining if there be a constriction ring, and you find unexpected resistance either to rotation or extraction the administration of Adrenalin will usually make the delivery an easy one. The question has been raised, Does the relaxation caused by Adrenalin predispose to postpartum hemorrhage? I have not encountered any such tendency, nor have I ever seen any ill effects from the use of Adrenalin. In an unanesthetized patient, Adrenalin will sometimes cause a disagreeable feeling of apprehension.

Subsequent Labors

I am under the impression that uterine inertia may recur at a subsequent labor, but I have never seen a constriction recur at a subsequent labor. Jeffcoate makes the statement that uterine efficiency improves with each pregnancy. "The prognosis for the second confinement depends largely on the degree of dilatation reached by the cervix in the first." If the child is delivered per vaginam, even if there be great difficulty, the next labor is more than apt to end in a spontaneous delivery. If, on the other hand, the child be delivered by cesarean section before the cervix has dilated, the next labor will probably be a difficult one.

Summary

The various forms of uterine dystocia are discussed. These vary from simple atony or uterine inertia to cervical dystocia and constriction ring. The type of incoordinate uterine action may vary from time to time in the same labor. The effect of these long labors upon the mother and baby is discussed, particularly when there is a constriction ring present. The best results for both mother and child are to be had by as prompt delivery from below as possible, i.e., when the cervix is dilated or almost fully dilated. If the patient is delivered by cesarean section before the cervix has dilated, the next delivery is apt to be difficult, although not so difficult as the first. A case is reported in which the constriction ring did not relax with Adrenalin and yet dramatically disappeared when amyl nitrite was used. In my last fifty-four cases with constriction rings, no baby was lost; the only mother lost in the entire series of 270 cases was before I began using Adrenalin in 1924.

References

1. The Seven Books of Paulus Aegineta, translated by Francis Adams, London, 1844, printed for the Sydenham Society, vol. 1, p. 646.
2. A Treatise on the Theory and Practice of Midwifery, London, 1779, Wm. Strahan, G. Nicol, vol. 3, p. 10.
3. Dewees, William P.: A Compendious System of Midwifery, Philadelphia, 1835, Carey, Lea, and Blanchard, vol. 2, p. 247.
4. Rigby, Edward: A System of Midwifery, Philadelphia, 1841, p. 335.

5. Denman, Thomas: An Introduction to the Practice of Midwifery, London, 1795, vol. 2, p. 28.
Collins, Robert: A Practical Treatise on Midwifery, London, 1835, Greene and Longman, p. 140.
6. Jeffcoate, T. N. A.: Canad. M. A. J. **58**: 42, 1948.
7. Rucker, M. P.: South. M. J. **18**: 412, 1925.
8. Sackett, N. B.: AM. J. OBST. & GYNEC. **42**: 248, 1941.
9. Woodbury, R. A., Hamilton, W. F., and Torpin, Richard: Am. J. Physiol. **121**: 640, 1938.
Woodbury, Torpin, Child, and Watson: J. A. M. A. **134**: 1081, 1947.
10. Reynolds, S. R. M., Hellmann, L. M., and Bruns, S. P.: Obst. & Gynec. Survey **3**: 629, 1948.
11. Rucker, M. P.: AM. J. OBST. & GYNEC. **52**: 884, 1946.
12. Rudolph, Louis, and Fields, Charles: AM. J. OBST. & GYNEC. **53**: 796, 1947.
13. Rudolph, Louis: J. A. M. A. **108**: 532, 1937.
14. Johnson, Herman W.: Texas State J. Med. **37**: 538, 1941.
15. Rucker, M. P.: J. Mt. Sinai Hosp. **14**: 576, 1947.
16. Eastman, N. J.: AM. J. OBST. & GYNEC. **53**: 432, 1947.
17. Reid, Duncan E.: AM. J. OBST. & GYNEC. **52**: 719, 1946.

THE USE OF SULFATHIAZOLE POWDER IN THE VAGINA IMMEDIATELY AFTER COMPLETION OF DELIVERY

CARL W. ROTTER, M.D., AND RAY H. LONG, M.D., CLEVELAND, OHIO

(From the Department of Obstetrics, Glenville Hospital and Booth Memorial Hospital)

A STUDY of the effect of sulfathiazole powder in the vagina immediately after completion of delivery was begun in 1946. The objective was to evaluate the effect of its use upon the morbidity of the early postpartum period with special reference to healing of episiotomy wounds and vaginal lacerations of various degree, the amount and type of vaginal discharge whether there had been any repair or not, the degree of pain in the perineum, and last, the influence upon the general well-being of the patient.

Preliminary Approach

In the first series of cases which preceded those in which the present method was adopted, the sulfathiazole powder was dusted into the episiotomy wounds and vaginal lacerations before suturing. This was done on alternate cases and the results obtained when compared with the controls showed a satisfactory improvement in most cases, yet there occurred instances where it appeared that delay in wound healing, which others had demonstrated by carefully controlled experiments, was taking place. To overcome this objection, it was felt that perhaps the powdered sulfonamide might be used as a barrier to any wound infection which could take place in the early postoperative period by placing it over the sutured wound instead of into it. When this was done the results were strikingly better than before.

Present Study

The procedure, which was adopted and used without further modification in the next 265 cases as well as in the final series of 214 cases which forms the basis for this study, is very easily performed. After the baby and placenta have been delivered and all the necessary repair completed and bleeding controlled to the satisfaction of the operator, the labia are separated with two fingers and 5 Gm. of sulfathiazole powder is instilled deep into the vaginal tract and spread down into the posterior fornix and about the cervix with the index and middle fingers. This maneuver has the additional advantage of being a final check for any sponge previously overlooked.

The intermediate series of 265 consecutive vaginal deliveries performed by the authors since the institution of this treatment terminated on June 15, 1948. Since this group included all vaginal deliveries, this meant that sulfathiazole powder was used in cases of episiotomy alone, episiotomy with various degrees and numbers of lacerations, lacerations alone, and, finally, those in which no laceration occurred.

The final series which forms the basis of the present comparison includes all vaginal deliveries performed at Glenville Hospital and Booth Memorial Hospital from June 15, 1948, to Aug. 1, 1948. This series consists of two groups: the first in which sulfathiazole powder was used, and the second in which no sulfonamide whatsoever was used in the vagina. The first group consists of all

the deliveries performed by the authors plus all the patients delivered by two other members of the Glenville staff and all the cases of one member of Booth Memorial staff. The second group is made up of all the patients delivered by the remaining members of both hospital staffs.

Observation and Comparison

All of the patients were checked daily and recordings made with special reference to the mode of healing of the perineum from the day of delivery until the patient left the hospital. At the same time, a daily record was kept of each patient's highest temperature elevation, the amount and odor of the lochia, the general well-being of the patient, and the amount of pain originating in the perineum.

In Table I is recorded the highest temperature reading during the entire hospital stay of all the patients who were critically studied during the six-week period beginning June 15 of this year, 1948. By comparing the highest temperature elevation in the two groups of cases, it appears that there is no striking improvement in the temperature curve through the use of sulfathiazole locally in the vagina immediately after delivery. Although there are a few scattered cases of higher temperatures recorded in the group in which sulfonamide was not used, it does not appear that the degree is great enough to draw any positive conclusions as to the effect of the local use of sulfonamide in reducing the possibility of general sepsis and fever in the immediate postpartum period, all other aspects of aseptic technique in the handling of the deliveries in both series of cases otherwise being equal. It does, however, indicate a very desirable trend if this discrepancy can be maintained to the same degree in subsequent series of cases.

TABLE I. HIGHEST TEMPERATURE OF EACH CASE DURING ENTIRE HOSPITAL STAY

NUMBER OF CASES IN WHICH SULFATHIAZOLE WAS USED	TEMP. ° F.	NUMBER OF CASES IN WHICH NO SULFATHIAZOLE WAS USED
1	98	1
4	98.2	3
5	98.4	2
22	98.6	43
9	98.8	20
20	99	26
6	99.2	10
5	99.4	7
2	99.6	6
1	99.8	1
4	100	4
1	100.2	1
0	100.4	1
0	100.6	0
0	100.8	1
1	101	1
0	101.6	1
0	101.8	1
0	102	1
0	103.2	2
0	104	1
Total 81		Total 133

The comparison of healing of the perineum of patients treated with 5 Gm. of sulfathiazole powder with those not so treated is given in Tables II and III. Out of 62 cases with episiotomy alone in the sulfonamide series, there were 12 cases, or 19.3 per cent, which developed redness and edema on one or more days. In the control group there were 30 cases, or 40.5 per cent of 74 patients, who had

TABLE II. HEALING OF PERINEUM—NO SULFATHIAZOLE POWDER USED

TYPE OF REPAIR	NUMBER OF CASES SHOWING GOOD HEALING	NUMBER OF PATIENTS DEVELOPING EDEMA AND REDNESS WITH POSTPARTUM DAYS OF OCCURRENCE RECORDED	SEPARATION OF WOUND AND GROSS INFECTION OCCURRED WITH POSTPARTUM DAY RECORDED
Episiotomy only 74	44	30	
		1 on 4th, 5th, and 6th days	
		2 on 4th and 5th days	
		3 on 6th and 7th days	→ Separated 8th day → Went home
		4 on 3rd and 4th days	
		5 on 3rd, 4th, 5th, 6th, and 7th days	
		6 on 3rd, 4th, and 5th days	
		7 on 4th day	
		8 on 4th day	
		9 on 3rd and 4th days	
		10 on 5th day	
		11 on 2nd day	
		12 on 5th day	
		13 on 3rd, 4th, 5th, 6th, and 7th days	
		14 on 3rd and 4th days	
		15 on 2nd, 3rd, 4th, 5th, and 6th days	→ Separated 6th, 7th, and 8th days → Went home
		16 on 5th day	
		17 on 3rd, 4th, 5th, and 6th days	
		18 on 4th day	
		19 on 4th, 5th 6th, and 7th days	
		20 on 5th and 6th days	
		21 on 3rd, 4th, 5th, and 6th days	
		22 on 4th and 5th days	
		23 on 3rd day	
		24 on 4th and 5th day	
		25 on 2nd day	
		26 on 4th day	
		27 on 3rd, 4th, and 5th days	→ Separated 6th, 7th, 8th and 9th days → Went home
		28 on 3rd day	
		29 on 3rd and 4th days	→ Separated 5th, 6th, 7th, 8th and 9th days → Went home
		30 on 2nd, 3rd, 4th, and 5th days	
No repair 48	47	1 on fifth day	
1° laceration only 8	6	1 on 3rd day 2 on 3rd, 4th, and 5th days	
2° laceration only 1	0	1 on 3rd and 4th days	
Episiotomy and laceration 2	1	1 on 2nd, 3rd, 4th, and 5th days	

TABLE III. HEALING OF PERINEUM—5 GM. OF SULFATHIAZOLE POWDER USED IN VAGINA

TYPE OF REPAIR	NUMBER OF CASES SHOWING GOOD HEALING	NUMBER OF PATIENTS DEVELOPING EDEMA AND REDNESS WITH POSTPARTUM DAYS OF OCCURRENCE RECORDED	SEPARATION OF WOUND AND GROSS INFECTION
Episiotomy only 62	50	12 1 on 4th, 5th, and 6th days 2 on 3rd day 3 on 2nd day 4 on 2nd day 5 on 2nd day 6 on 1st and 2nd days 7 on 1st and 2nd days 8 on 3rd day 9 on 3rd day 10 on 1st day 11 on 1st, 2nd, 3rd, and 4th days 12 on 2nd and 3rd days	None
No repair 14	14	None	None
1° laceration only 4	3	1 on 4th day	None
2° laceration only 0	–	–	–
Episiotomy and laceration 1	1	1 on 4th day	-

TABLE IV. AMOUNT AND ODOR OF LOCHIA IN POSTPARTUM PERIOD

	AMOUNT OF LOCHIA			ODOR OF LOCHIA		
	SLIGHT	MODERATE	PROFUSE	NONE	SLIGHT	FOUL
5 Gm. sulfathiazole powder used	11	54	16	35	43	3
No sulfathiazole powder used	15	47	71	15	65	53

poor healing and, in addition, there were four instances of wound separation as compared to none in the group treated with sulfathiazole. The mode of healing in the patients who had first- or second-degree lacerations only was satisfactory in both series and because of the rather small number of cases in these groups, no other deduction can be made at this time.

One of the most obvious differences in the two groups of cases which was noted very early after this procedure was added to the routine of delivery was the decrease in the amount of lochia and the great decrease in the amount of odor. Whereas medically these factors had no particular significance other than convenience to both patient and nurses, the fact cannot be overlooked that from the esthetic standpoint the very notable decrease in offensive odor of the lochia makes a world of difference to everyone concerned. In Table IV is shown the rather marked difference in the preponderance of cases with profuse discharge in the nonsulfathiazole-treated cases. There were 71 patients out of 133, a percentage of 53.3 per cent, who had a profuse amount of lochia on one or more postpartum days as compared to the treated group which had 16 patients out of 81, or 19.7 per cent. Of those with a slight amount of lochia, there were 15 in the nontreated group, or 11.3 per cent, as against 11 in the other, or 13.6 per cent. In the ones with a moderate amount of discharge, the distribution was 66.7 per cent in the treated and 35.4 per cent in the other. It may be concluded that there was a definite suppression in the amount of lochia in the treated cases. But from the standpoint of nicety and refinement it may be stated that the simplicity of performance and the almost negligible element of time required in the added procedure as well as the minimal expense involved is a small outlay for the marked suppression of the offensive odor of the lochia which is realized. There were only three patients, or 3.7 per cent, who had foul lochia on one or more postpartum days in the treated group as compared to 53 patients, or 39.8 per cent, in the nontreated. Of those with absence of foul odor there were 35 patients, or 43.2 per cent in the treated, as compared to 15 or 11.3 per cent in the nontreated. Those with slightly foul lochia were 53.1 per cent in the treated and 48.9 per cent in the control.

TABLE V. GENERAL CONDITION OF PATIENT

	FAIR	GOOD
Sulfathiazole group	2	79
No sulfathiazole group	19	114

Regarding the general well-being of the patient, it may be noted in Table V that there were only two patients who were considered fairly good as compared to 79 who were good in the treated group, whereas in the nontreated group 19 were fairly good and the remaining 114 were good. It is admitted that by this process of evaluation of the general condition of the patient it is more difficult to arrive at an accurate appraisal in every instance, but the much better showing in the treated group is indicative of the fact that the favorable influence of the other factors, as has been demonstrated, is reflected in the condition of the patient as a whole.

When comparing the amount of pain arising in the perineum alone and for which medication was necessary, the largest series of patients needing relief were found among those who had episiotomies performed upon them. In this category there were 62 patients with episiotomy upon whom sulfathiazole was used. Out of this number, 20, or 32.2 per cent, needed medication on one or more postpartum days for the control of pain as shown in Table VI. Of the 87 cases of episiotomy in which no sulfathiazole powder was instilled into the vagina,

there were 48, or 55.2 per cent, who needed medication for relief. There were two patients with laceration alone in the nonsulfathiazole group who needed medication for pain while none of the sulfonamide group had to have medication for perineal pain. In addition, there were two with episiotomy and laceration in the control group who needed relief for pain whereas there were none in the treated group.

TABLE VI. DEGREE OF PAIN IN PERINEUM

	NO REPAIR		EPISIOTOMY		LACERATION		EPISIOTOMY AND LACERATION	
SULFATHIAZOLE USED	YES	NO	YES	NO	YES	NO	YES	NO
No pain	5	19	5	6	3	5	0	0
Pain but no medication given	4	10	37	33	4	4	3	4
Medication given for pain	0	0	20	48	0	2	0	2

History and Review

The use of local concentration of sulfonamide compounds inserted into wounds by Hawking did not produce necrosis in experimental wounds and only very slight depression of fibroblast formation. This was confirmed by Chambers, Harris, Schumann, and Ferguson. The chief theoretical disadvantage of the use of sulfathiazole is its tendency to clump and form insoluble masses which remain as foreign bodies in the tissues. As compared to sulfanilamide, the drug is much less soluble in water solution or in serum. The relatively low solubility may be an advantage in that the drug persists in situ for a longer period and it may be concluded that probably the optimum combination of high concentration plus sufficient duration is greater with sulfathiazole when compared to sulfanilamide, sulfapyridine, or sulfadiazine. By using sulfathiazole locally in this manner a dual purpose is accomplished. There is suppression of bacterial growth in the ideal culture medium provided by the lochia, as well as the formation of a barrier to the bacteria at the wound entrance during the first critical period when the healing process seals the wound sufficiently to enable complete healing to take place without the complicating factor of infection.

The pathogenic organisms commonly found in the vagina against which sulfathiazole is effective in varying degrees are the beta hemolytic streptococcus, staphylococcus, pneumococcus, gonococcus, colon group, *Proteus vulgaris, Clostridium perfringens, Clostridium septicum, Clostridium oedematiens,* and even in a measure the tetanus bacillus. Those against which it is ineffective are *Bacillus proteus,* most of the *Streptococcus viridans* groups and most viruses. Therefore, it then becomes apparent why the results following its use have been uniformly good, since even in the cases when no gross break in the continuity of the mucosa or skin has occurred there is, nevertheless, tissue susceptibility to infection due to the varying degrees of trauma incident to the compression, abrasion, and stretching of tissues which result during the process of delivery.

Fahraeus showed that instillation of two suppositories each containing 0.5 Gm. of sulfanilamid-thiazole every 12 hours from admission until the fifth puerperal day in 212 primiparas delivered of full-term or premature babies compared very favorable with a control group of 217 of the nontreated patients.

Ackman and Wilson used an emulsion of finely powdered sulfathiazole 5 per cent in a mix of 2 per cent triethanolamine, 24 per cent distilled water, 5 per cent white beeswax, and 64 per cent liquid paraffin impregnated in a pack and placed in the vagina following surgery with very good results.

Manuel found sulfanilamide solution for douche together with sulfonamide internally very efficacious for vaginal infection.

Siegler developed a 10 per cent sulfathiazole in acid-base jelly for the treatment of vaginitis and cervicitis with which response to treatment was excellent whether the vaginitis was trichomonal, monilial, or nonspecific in origin. He reports sixteen failures in which the infection was due primarily to trichomonas and two to monilia.

Similar good results were obtained by Roblee, who used sulfathiazole incorporated in an acid jelly base in treating various types of cervicitis and vaginitis.

Discussion

The use of sulfathiazole powder locally in the vagina immediately following delivery has three advantages over other methods of sulfonamide application previously advocated. In the first place, there is the ready accessibility of the 5-Gm. package of sterile sulfathiazole powder. Second, no special type of applicator is necessary to instill the powder into the vagina. The labia are merely separated with the fingers, the powder poured in and evenly distributed throughout the vagina and about the cervix. Third, it is one operation, quickly accomplished in a few seconds with no further work or procedure necessary.

There is, in addition, the consideration of possible allergic reactions to the use of this drug. Local allergy to the drug was anticipated, but to date no untoward reactions have been noted which might be interpreted in this light. In view of the experience to date, it appears that any unpleasant reactions to the drug will be extremely uncommon if they will occur at all under the conditions of this particular method of use. The blood level of sulfathiazole from absorption through the vaginal mucosa is negligible. It may therefore be assumed that adverse systemic reactions to such use of sulfathiazole may be disregarded altogether. The benefits derived from the use of this procedure in the management of all vaginal deliveries are most welcome, while at the same time no contraindications have appeared which would tend to make its use undesirable.

Summary and Conclusions

1. The prophylactic use of sulfathiazole powder in the vagina as a last step in the performance of vaginal delivery is described.

2. There is a definite suppression in the amount of lochia in the treated cases.

3. There occurs a marked suppression of offensive odor of the lochia in the patients treated by this method.

4. Redness and edema of episiotomy wounds occurred in 19.3 per cent of sulfathiazole-treated patients as compared to 40.5 per cent in the nontreated group.

5. No case of wound disruption has occurred in the series where sulfathiazole was used whereas it occurred four times in the control series.

6. There was a tendency toward lesser temperature elevation in the treated group.

7. Pain, especially in patients who had episiotomies, was severe enough to necessitate medication in 32.2 per cent of the treated group as compared to 55.2 per cent of the nontreated group.

8. The general condition of the patients in the treated group was found to be better than in the control group.

9. The lack of any allergic reactions to the use of sulfathiazole powder as described in this procedure has been noted in a total of 346 cases to date.

References

1. Ackman, D., and Wilson, G.: Canad. M. A. J. **46**: 209-214, 1942.
2. Chambers, L. A., Harris, T. N., Schumann, F., and Furguson, L. K.: J. A. M. A. **119**: 324-327, 1942.
3. Fahraeus, R.: Gynaecologia **124**: 1-10, 1947.
4. Manuel, E.: Antiseptic **41**: 605-607, 1944.
5. Siegler, S. L.: Am. J. Obst. & Gynec. **52**: 1-13, 1946.
6. Hawking, F.: Lancet **1**: 786, 1941.
7. Kennedy, R. H.: Connecticut M. J. **6**: 9-14, 1942.
8. Key, J. A.: South. M. J. **35**: 55-58, 1942.
9. Hawking, F., and Piercy, J. E.: Brit. M. J. **1**: 511, 1941.
10. Brunner, W., and Schlaffer, E.: Schweiz med. Wchnschr. **7**: 213, 1941.
11. Roblee, M. A.: Am. J. Obst. & Gynec. **46**: 400, 1943.

628 East 185th Street

CARCINOMA OF THE CERVIX CONCOMITANT WITH PREGNANCY

MARVIN G. SADUGOR, M.D., JAMES P. PALMER, M.D., AND
MELVIN C. REINHARD, M.A., BUFFALO, N. Y.

(From the Roswell Park Memorial Institute)

CONCOMITANT malignancy of the uterine cervix and pregnancy are considered to be a comparatively rare combination. This is necessarily so when one realizes that the age distribution for pregnancy is declining and is at a low level for the age period when the cervix malignancy age distribution is beginning to increase and that the overlap of the two curves represents a small portion of the entire age distribution of cervix cancer.

Maino and Mussey[1] have reported 0.7 per cent of coexistent cervix malignancy with pregnancy in 3,750 cases of cancer of the cervix. Danforth,[2] from another point of view, reports that in 10,000 pregnancies there were 0.032 per cent with cervix malignancy.

Although the incidence is comparatively low, it represents a complication which must be born in mind constantly as a possibility when the symptom of painless bleeding is present during pregnancy. This aspect has been emphasized by Strauss,[3] Kobak et al.,[4] Willson,[5] Maino and Mussey,[1] and others.

Case Material Studied

A review of 4,652 cases of carcinoma of the cervix admitted to this institution during the years 1917 to 1947 shows that 124 or 2.6 per cent were pregnant or had been pregnant within one year preceding admission. The selection of one year preceding admission is arbitrary, but because of the reasons below, it seemed reasonable to conclude that the two conditions were coexistant within that period.

1. The majority of the associated cases were in the far-advanced stages, and corresponded with the stages of the coexistant group.

2. In most instances, the carcinoma was diagnosed as such within a short interval following pregnancy.

3. A review of the case histories revealed the fact that nearly all had symptoms of bleeding or bloody vaginal discharge before, during, and immediately following pregnancy.

We feel that this information indicates almost incontrovertibly that the carcinoma was present before or occurred during pregnancy.

The breakdown of the 124 cases into the status of the two conditions shows that 36 cases were pregnant at the time of admission. In the remaining 88 cases, carcinoma of the cervix was diagnosed during the postpartum period which ranged from two weeks to one year, the majority in less than three months.

Age.—It is a well-known fact that carcinoma of the cervix is essentially a disease of the middle years and its frequency increases rapidly after age 35, reaching a peak at 47 years of age. Sadugor and Palmer[6] found it to be still relatively common until age 65, after which there was a gradual decrease in the incidence. Pregnancy, on the other hand, decreases rapidly after the age 35. Therefore, in dealing with cases of pregnancy complicated by cancer of the cervix, we find a younger age group of patients and therefore a much lower incidence of these two jointly.

Approximately 22 per cent of the cases occurred before age 30, 62 per cent occurred between ages 30 and 40, while 15 per cent occurred after age 40. This illustrates the fact that carcinoma of the cervix during pregnancy reaches its maximum occurrences during the 30 to 40 age group. The average age of these patients was 33.9 years, the youngest being 18, and the oldest 45 years of age.

Gravidity and Stage of Pregnancy.—In 14, or 11.2 per cent, of the cases, carcinoma occurred in the first pregnancy, giving a ratio of multipara to primipara of approximately 8:1, whereas in normal pregnant patients, the ratio is about 5:3. There was an average of five pregnancies per patient in this series. The greatest number of pregnancies in any one case was 13.

The entire series showed that in the first trimester of pregnancy there were 39 cases, three of which were one month pregnant. During the second trimester, there were only 11 cases, the remaining 73 cases occurring in the last trimester, 59 of whom had full-term pregnancies. One case from the group had carcinoma of the cervix complicated by an ectopic pregnancy. Our five-year survivals with no evidence of disease showed no cases in which the disease was diagnosed in the second trimester. In the first trimester, 22.2 per cent and in the last trimester, 26.5 per cent of the cases survived five years with no evidence of the disease. The cases in this last group were all term pregnancies, while in Maino and Mussey's[1] series of cases there were no cases that had carcinoma of the cervix at term that survived five years. The carcinoma of the cervix coexistant with ectopic pregnancy also survived five years.

Symptoms and Their Duration.—The significant manifestations of carcinoma of the cervix during pregnancy are the usual symptoms of carcinoma of the cervix modified by those of pregnancy. The initial symptoms and also the most common were vaginal bleeding, found in 73 per cent of the cases and abnormal vaginal discharge (purulent, watery, or bloody) in 19 per cent of the cases. The bleeding under these circumstances is characteristically painless and may be profuse or merely spotty. It may be irregular or progressive in amount. Abnormal discharge, which may become watery, purulent, or foul, may be a late symptom, as well as loss of weight, pain, and palpable metastatic extension. Unfortunately, carcinoma of the cervix may be a silent clinical entity with no symptomatology as was seen in eight per cent of our cases, the cancer being discovered during routine examination.

The duration of symptoms was found to be much shorter in this series of cases than in that of a group of cases of carcinoma of the cervix without pregnancy. This may be accounted for by the fact that the patient is more likely to be concerned about her condition during pregnancy than she would be normally. Ironically, many of the patients had symptoms of vaginal bleeding or discharge for periods ranging from one to nine months before the correct diagnosis was made and the patient referred here for treatment. These manifestations are often misinterpreted when the neoplasm is associated with pregnancy because they may represent a threatened abortion or ectopic pregnancy during the first trimester, and placenta praevia, or premature separation of the placenta during the last trimester of pregnancy. But we would like to stress the point that has been brought out innumerable times in the literature that should these symptoms present themselves, the obstetrician or gynecologist, in order to establish a differential diagnosis, should overcome the persistent fear of interrupting the pregnancy by performing a thorough, sterile pelvic examination during any stage of pregnancy and institute the necessary diagnostic procedures to rule out the presence of any coexistant malignancy. Obviously, in this way, carcinoma of the cervix, coincidental with pregnancy, can be detected in its early stages and as a result effective therapy may be employed leading to more favorable results.

Type of Lesion.—There were 120 cases of squamous carcinoma of the cervix in this series, the remaining four cases were two adenocarcinomas and two adenoacanthomas. The latter four cases died of disease or incidental complications in less than five years.

Treatment.—The treatment of cancer at this Institute has been entirely radiological, as is the case with cervical cancer as a whole. Although the technique and dosages have varied considerably during the interval of this report, the general plan has remained more or less constant. We feel that cases diagnosed as carcinoma of the cervix during pregnancy up until viability is certain, should be treated without regard for the fetus, since any appreciable delay might markedly decrease the mother's chances of survival. If the diagnosis has been delayed until viability is probable, we feel that the patient should have cesarean section without hysterectomy and should be started on radiation therapy as soon as her general condition permits (ten days to two weeks).

Usually spontaneous abortion occurs at about the end of the third week of external radiation and usually this interval has been sufficient for the local infection (secondary to the ulceration of the growth) to be markedly reduced, thus keeping postpartum infection to a minimum. Very little radiation fibrosis has occurred during this interval so that serious lacerations are infrequent.

The choice of this plan seems to be substantiated by Heyman,[7] who shows that when an induced abortion or section (simple or Porro) was used prior to radiation, only 11.1 per cent survived five years with no evidence of disease whereas subsequently, in a group of cases in which radiation was used and the patient was allowed to abort spontaneously, he obtained a 57 per cent five-year cure rate.

Occasionally, with a bulky growth which does not regress sufficiently with external radiation, spontaneous delivery is difficult or impossible and the dead fetus may necessarily have to be delivered by hysterotomy.

We feel that this plan, whereby the uterus remains, allows a more nearly adequate distribution of intracavitary radiation and also fewer post-treatment bladder and rectal complications. This is in agreement with Kobak et al.,[4] Beck,[8] Titus,[9] and McNeil.[10]

Our radiation treatment consists of external radiation (x-ray), 400 to 500 r. to one port daily, or 100 to 150 r. to each of four ports daily for a total of approximately 4,000 r. within 45 days. The dosage to the tumor area depends considerably on the size of the patient. Immediately following completion of the external irradiation, intracavitary radium is given in one treatment period, lasting from 50 to 100 hours, depending upon the size of the patient and amount of radiation from the external radiation previously delivered to the tumor area. We attempt to give on the average 8,500 to 9,000 r. combined x-ray and radium "r.," to a point 2 cm. lateral to the cervical canal, of which on the average about 50 per cent of the total is given by each of the two methods of radiation. Under this plan of treatment, approximately 5,000 combined r. is delivered to a point 5 cm. lateral to the cervical canal, which in the average case approximates the junction of the broad ligaments with the lateral pelvic wall.

End Results of Treatment.—In order to determine whether or not the complication of pregnancy influences the cure rate of squamous-cell carcinoma of the cervix, a preliminary survey was made of the end results of the group of patients with pregnancy (designated as Group I) and compared with the end results of another group of patients which comprised all of the cervix cases including the pregnancy cases treated at this institution during the years 1917 to 1942 inclusive (designated as Group II). No patients of either group admitted subsequent to 1942 were included in this survey. This afforded an opportunity to compare end results on a minimum of five-year survival.

All cervix cases were classified according to the League of Nations recommendations and since it is recommended that all patients who received treatment for their malignancy elsewhere prior to admission here be eliminated, we have excluded 17 patients who fall into this category. Thus, by eliminating the patients treated subsequent to 1942 and those who received treatment prior to admission, the number of pregnancy cases to be compared with the group as a whole has been reduced to 78.

Although we are not comparing two comparable groups because the age distribution is markedly different, yet, because further elimination would still further reduce a comparatively small sample, a preliminary study of the end results of these two groups was made.

The breakdown of the two groups into clinical stages and end results of each stage, as well as the over-all survival is shown in Table I. It can be noted that there is no significant difference in the survival rate of the two groups, either in the individual stages or in the collective survival of 26.9 per cent for Group I and 27.5 per cent for Group II. Fortunately, the distribution of the cases into the various stages of the disease is essentially the same for both groups and the collective survival rates may be compared directly. Had there been a preponderance of the cases in any one stage, the results could not have been compared directly. We have, therefore, tentatively concluded from the preliminary breakdown that insofar as the ultimate cure rate is concerned, pregnancy does not influence the end results.

TABLE I

CARCINOMA OF THE CERVIX ASSOCIATED WITH PREGNANCY, 1917 TO 1942 INCLUSIVE

	STAGE	NUMBER TREATED	PER CENT OF TOTAL	5-YEAR SURVIVAL NUMBER	FREE OF DISEASE PER CENT
Group I	I	9	11.5	6	66.6
	II	19	24.4	8	42.1
	III	28	35.9	6	21.4
	IV	22	28.2	1	4.5
	Total	78		21	26.9

ALL CERVIX CASES—1917 TO 1942 (INCLUDING PREGNANCIES)

	STAGE	NUMBER TREATED	PER CENT OF TOTAL	5-YEAR SURVIVAL NUMBER	FREE OF DISEASE PER CENT
Group II	I	304	9.3	198	65.1
	II	833	25.6	375	45.0
	III	1093	33.6	290	26.5
	IV	1021	31.4	32	3.1
	Total	3251		895	27.5

A more rigorous examination of the data required further elimination. The radiation technique had become standardized in 1933; therefore, only the cases admitted from 1933 to 1942 were considered in both groups and since age does influence the end results in carcinoma of the cervix, increased age being associated with increased life expectancy, only those patients were used in Group II who were 45 years of age or younger. Thus, in Table II the five-year end results of two comparable groups of cases, 48 cases of pregnancy and 702 nonpregnant cervix cases from 1933 to 1942 are presented. Here, again, it can be seen that the stage distribution is essentially the same for the two groups and that the survival rate too is essentially the same for the various stages. However, the number of cases in the various stages in Group I are too small for comparison. The over-all figure of 32.9 per cent for Group II and 37.5 per cent for Group I cases

would seem to indicate a better survival in this last consideration. However, when these values were considered statistically, it was found that the two values do not differ significantly and no importance may be attached to this apparent difference.

TABLE II

PREGNANCIES, 1933 TO 1942 INCLUSIVE, AGES 20 TO 45 YEARS

	STAGE	NUMBER TREATED	PER CENT OF TOTAL	5-YEAR SURVIVAL NUMBER	FREE OF DISEASE PER CENT
Group I	I	6	12.5	4	66.6
	II	17	35.4	8	47.0
	III	18	37.5	5	27.8
	IV	7	14.6	1	14.3
	Total	48		18.0	37.5 ± 6.98%

NON-PREGNANT CERVIX CASES, 1933 TO 1942 INCLUSIVE, AGES 20 TO 45 YEARS

	STAGE	NUMBER TREATED	PER CENT OF TOTAL	5-YEAR SURVIVAL NUMBER	FREE OF DISEASE PER CENT
Group II	I	100	14.2	68	68.0
	II	244	34.8	108	44.2
	III	225	32.0	49	21.8
	IV	133	18.9	6	4.5
	Total	702		231	32.9 ± 1.76%

The 17 pregnancy patients previously excluded because of treatment prior to admission here showed a five-year survival free of disease of 5.9 per cent. Since the prior treatment elsewhere was predominantly surgical and since the survival is considerably less than that in the group treated here radiologically (5.9 per cent as compared with 26.9 per cent), it seems reasonable to conclude that radical surgical interference is not the proper method of treatment, in which we concur with Heyman.[7]

Summary

One hundred twenty-four coexisting and associated cases of carcinoma of the cervix and pregnancy were studied and five-year end results presented.

The results show almost identical cure rate with carcinoma of the cervix unassociated with pregnancy for the same time interval within the comparable age groups.

Our figures and others tend to show definitely better results when conservative treatment is used than when radical surgery is performed prior to irradiation.

The distribution of clinical stages of carcinoma of the cervix associated with pregnancy is almost identical with the nonpregnant cases. This shows that prenatal and postpartal examinations have been neglected and as a result the disease has not been discovered in its early stages. It is recommended that all patients showing any abnormal symptoms during pregnancy should have a thorough vaginal examination, regardless of the stage of pregnancy. All postpartal cases should have repeated examinations after the structures have returned to normal. We believe that such examinations would result in such patients receiving treatment during the early stages of the disease and the cure rate would be definitely improved.

References

1. Maino, C. R., and Mussey, R. D.: Am. J. Obst. & Gynec. 47: 229, 1944.
2. Danforth, W. C.: Am. J. Obst. & Gynec. 34: 365, 1937.
3. Strauss, A.: Am. J. Roentgenol. 43: 552, 1940.
4. Kobak, A. J., Fitzgerald, J. E., Freda, Vincent C., and Rudolph, L.: Am. J. Obst. & Gynec. 49: 307, 1945.
5. Willson, J. Robert: Am. J. Obst. & Gynec. 50: 275, 1945.
6. Sadugor, M., and Palmer, J. P.: Am. J. Obst. & Gynec. 56: 680, 1948.
7. Heyman, J.: J. A. M. A. 135: 412 (October 18), 1947.
8. Beck, A. C.: Obstetrical Practice, ed. 3, Baltimore, 1942, Williams and Wilkins Company, pp. 615-616.
9. Titus, P.: The Management of Obstetric Difficulties, ed. 2, St. Louis, 1940, The C. V. Mosby Company, pp. 163-166.
10. McNeil, Wm., Jr.: Am. J. Obst. & Gynec. 30: 414, 1935.

PROLAPSE OF THE UTERUS AND PREGNANCY*

ARTHUR H. KLAWANS, M.D., AND AARON E. KANTER, M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology, University of Illinois College of Medicine [Rush Faculty], the Presbyterian Hospital, and the Department of Gynecology, Mount Sinai Hospital)

PROLAPSE of the uterus and pregnancy are infrequently associated conditions. Only 170 cases were culled from the literature by Kibel[1] in 1944 and a scattered few have been reported since then. The rarity of the coexistence of these two conditions is reflected by the statistics of Kibel, who reports a ratio of 1 to 15,696 deliveries at Bronx Hospital and by Keettel,[2] who found 1 case in 13,000 deliveries at University Hospital in Iowa City. In most previously reported instances, pregnancy was superimposed upon pre-existing prolapse of varying degree and the condition was obvious early in the pregnancy. We are reporting on four cases of combined prolapse and pregnancy, two of these showing the prolapse relatively late in the gestation. Since the condition under consideration is uncommon and no full agreement as to treatment can be found in the reports of previous authors, we have set out to cite our cases and to suggest a rationale for conservative and successful treatment of this combination of factors.

Case Reports

CASE 1.—Mrs. C. F., aged 31 years, was first seen on May 6, 1946. Her last regular menstrual period was on Jan. 11, 1946, and she had felt well throughout the intervening period. She had had one previous full-term pregnancy that terminated in a sixty-five hour labor with a difficult forceps delivery, three years before. The past history was irrelevant except for an appendectomy in 1933. Physical examination at this time revealed a pregnancy reaching to three fingerbreadths below the umbilicus, a moderately flat pelvis, and an otherwise healthy, albeit thin, individual. Except for a hypotension (98/60), all laboratory tests were within normal limits. Pregnancy progressed uneventfully until Sept. 11, 1946, when the patient called and reported that there had been a sudden appearance of a mass at, and through the vulva. The patient was immediately hospitalized. Examination revealed a purplish blue, edemtous, angry-looking mass, 5 cm. in diameter, protruding about three inches outside the vulva. Vaginal examination under sterile precautions was done immediately and the mass felt was determined to be cervix uteri with the uterus itself lowered to the point where the lower uterine segment and the contained fetal head were practically resting on the perineum. The uterus was gently pushed up into the abdomen and the cervix returned to the vagina. The patient was put to bed in a slight Trendelenburg position and during the period of bed rest, a matter of a few days, the condition remained alleviated. Examination of the cervix by means of a vaginal speculum revealed a normal-appearing organ which had lost all of its edema and discoloration. The patient was sent home and told to remain in bed. After one week, with the condition remaining as it was on leaving the hospital, she was allowed out of bed and in a few days the prolapse recurred. After several weeks of in-bed and out-of-bed

*Read before a meeting of the Chicago Gynecological Society, March 19, 1948.

treatment, it was felt that some more satisfactory method of keeping the cervix within the vagina was necessary because it was imperative that this patient tend her child and her home. On October 10, a Smith-Hodge type pessary No. 5 was inserted after returning the uterus to its normal position. This held the organs in place and it was possible for the patient to be up and about at her duties with no discomfort and no restrictions. After one week, she was re-examined and it was again found that the cervix was normally high in the vagina and that its appearance was normal.

On October 18, the estimated "due date," the patient had spontaneous onset of labor, pains beginning at 6 A.M. She was admitted to the hospital at 12:45 P.M. with contractions every fifteen minutes and the cervix dilated two fingerbreadths. Labor progressed slowly because of poorly developed, infrequent contractions. At 4 P.M. pains were occurring every four minutes and were only of moderate severity. At this time vaginal examination was done and it was found that the cervix was dilated 2½ fingerbreadths. The membranes were artificially ruptured. Soon after this the contractions became more frequent and more severe but dilatation still progressed slowly. At 5:45 P.M., 100 mg. of Demerol were given intramuscularly. Dilatation began to be apparent very soon after this, so that at 6:45 it was found to be four fingerbreadths. The pessary was removed at this time. Spontaneous delivery of a female infant weighing 6 pounds, 5¾ ounces was accomplished at 7:30 P.M. and the placenta expressed at 7:35 P.M. Total length of labor was 13 hours, 35 minutes. Old bilateral cervical lacerations were freshened and repaired. The pessary was then reinserted. The postpartum course was entirely normal, with no febrile reaction at any time. The patient was discharged on October 26. On November 30, 1946, she reported for her postnatal examination. The pelvic organs were found to be in a normal multiparous condition with the repaired cervical lacerations perfectly healed. At re-examination on January 13, 1947, the pessary was removed and the only abnormal finding was that of a slight cystocele. The uterus could not be brought down by the patient's efforts, and the cervix was normal in appearance. To date, the condition has remained the same.

CASE 2.—Mrs. E. P., 29 years of age, was first seen in this pregnancy on June 5, 1946. Her last menstrual period began on March 21, 1946. One previous pregnancy had been terminated with outlet forceps and episiotomy on Sept. 21, 1942, after fourteen hours of labor. General physical and laboratory examinations at this time were negative, a diagnosis of early pregnancy was made. Gestation progressed in a normal manner until Sept. 15, 1946, when the patient telephoned to state that there was a protrusion from the vagina. She was advised to go to bed but this was of no avail.

On examination it was found that the cervix was protruding some 2½ inches from the vulva and was purplish red, edematous, and oozing blood from its edges. The uterus was returned to its position manually and the cervix returned into the vagina. A Smith-Hodge type pessary No. 5 was inserted and the uterus stayed in place perfectly. The patient experienced no discomfort and immediately was able to be about her business unhampered. Pregnancy progressed normally and the patient went on until Jan. 11, 1947, when it was decided to try induction of labor because of a calculated two-week postmaturity. At the time that induction was begun the cervix was already two fingerbreadths dilated. Induction was instituted by rupture of the membranes and the use of two doses of Calgluquine, 2.5 c.c. each, at one-hour intervals. Two and a half hours after the rupture of the membranes, and one and a quarter hours after the onset of labor, dilatation reached 4½ fingerbreadths and the pessary was removed. Fifteen minutes later, spontaneous delivery of a male infant weighing 9 pounds, 13¾ ounces was accomplished with the aid of an episiotomy. The placenta was expelled two minutes after the delivery of the baby. The episitomy was repaired and the pessary reinserted. The postpartum course was entirely afebrile and without event. The patient was discharged from the hospital on the eighth postpartum day.

On February 22 the patient reported for postnatal examination. The pelvic organs had involuted to the point where all seemed to be in normal condition except for the presence

of a moderate cervical erosion. The patient was re-examined one month later and the pessary was removed. The cervical erosion was treated by cauterization. All of the pelvic organs gave a normal multiparous appearance without even cystocele or rectocele being present. On healing of the erosion the patient was discharged.

CASE 3.—Mrs. J. M., aged 24 years, was first seen on July 16, 1946, with early pregnancy and prolapse of the uterus. Her last period was on April 8, 1946. This was her second pregnancy, her first having terminated Oct. 15, 1944, and the protrusion of the cervix had been present since that time. Physical and laboratory examinations were negative except for the pregnancy and the prolapse. It was felt that when pregnancy had progressed to the point where the uterus was pulled up into the abdomen, the cervix would be pulled up into the vagina and the prolapse cured for the duration of the pregnancy. This did not take place. On October 25 the prolapse was so annoying and the cervix had taken on such a great amount of edema and irritation that the discomfort from it and the appearance of it were alarming. A Smith-Hodge type pessary No. 5 was inserted and the uterus and cervix put into place. This position was maintained with complete comfort and rapid return of the appearance of the cervix to normal. Labor began spontaneously on Jan. 22, 1947, and after dilatation had progressed to four fingerbreadths, sterile vaginal examination was done, the pessary was removed, and the membranes were ruptured. Thirty-five minutes later the patient was delivered, spontaneously, of a female infant weighing 7 pounds, after a five-hour labor. Instead of using the pessary puerperally, a vaginal pack was inserted and removed in twenty-four hours. At the time of her postpartum examination on March 14, 1947, the prolapse still was found to exist and was treated subsequently by surgery.

CASE 4.—Mrs. A. C., 33 years of age, was first seen on April 8, 1947. She had had two previous pregnancies with a prolapse of the uterus dating from the last of these. Her last regular menstrual period had begun on Feb. 1, 1947, and her expected date of delivery was estimated to be about Nov. 8, 1947. A Smith-Hodge type pessary was inserted into the vagina on the first examination and left in place until May 15, 1947, when it was felt that the size of the uterus would act to maintain that organ as an abdominal organ and relieve the prolapse until at least after delivery. The prolapse recurred almost immediately and the patient developed an incarceration of the uterus with an overdistention of the bladder and paradoxical incontinence. After emptying the bladder of 1,000 c.c. of urine, the prolapse was replaced and the pessary reinserted. All discomfort stopped at once and the patient remained comfortable throughout the remainder of the pregnancy.

On Nov. 13, 1947, at 4:30 A.M., labor began. The patient entered the hospital at 6:30 A.M. with pains occurring at five-minute intervals. Sterile vaginal examination was done at 7:50 A.M. and the cervix was found to be completely dilated. The pessary was removed, the membranes were ruptured artificially and the patient delivered spontaneously at 8:08 A.M. The placenta was expressed at 8:09 A.M., a total labor of three hours, thirty-nine minutes. The pessary was reinserted. Except for a moderate postpartum hemorrhage, the puerperal period was entirely comfortable and without event.

The patient reported for postnatal examination on Jan. 12, 1948, at which time the uterus was well held in place, well involuted, and the cervix was found to be clean. The pessary was removed and the uterus showed no tendency to prolapse. In a subsequent telephone report the patient stated that the cervix had descended somewhat but did not protrude from the vulva.

Discussion

Prolapse of the uterus is most commonly seen in women who have had pregnancies and deliveries which had been more or less responsible for the descensus. In order for prolapse to take place, there must be relaxation and tearing down of the structures which are charged with the task of supporting

the uterus. In such a situation, the softening and stretching of the pelvic supporting structures associated with a pregnancy would act to aggravate and make more marked any prolapse condition. The supporting structures affected when prolapse exists are the cardinal ligaments, the pubocervical ligaments, the uterosacral ligaments, the fascias of the pelvic floor, the vaginal and perineal tissues, and, perhaps slightly, the round ligaments.

From a purely obstetric viewpoint, prolapse of the uterus may be responsible for several types of difficulty. Sterility may be the result of such a condition because a pool of semen cannot be deposited around a cervix that protrudes from the vaginal introitus and because the prolapsed uterus may fill the vagina and prevent copulation. Abortion may be produced as a result of the trauma and vascular congestion that exist in a prolapsed uterus that contains a pregnancy. Infection can readily result when the protruding highly vascular and easily injured cervix is subjected to trauma over a rather long period of time. Finally, cervical dystocia is commonly associated with prolapsed uterus.

When prolapse of a degree exists before pregnancy takes place, it is to be expected that the condition of uterine descensus will be aggravated by the changes that take place in the tissues as a result of the pregnancy. This condition will remain annoying or incapacitating until such a time as the pregnancy has progressed sufficiently to raise the uterus into the abdomen and pull the cervix up into the vagina. This effects an apparent cure of the prolapse which lasts until the pregnancy is completed. Following this, the pre-existing condition returns, probably to a worse degree than before the pregnancy. This pattern is followed by the majority of patients, but occasionally a prolapse will not be pulled up as the pregnancy progresses and the condition will be evident throughout the gestation. This has necessitated patients being kept in bed for varying lengths of time even up to the entire course of pregnancy. Where prolapse is allowed to exist throughout the pregnancy with just the aid of postural relief, the patient comes to labor with an existing prolapse and the great difficulties reported in the literature may result. It is in such patients and in those in whom the prolapse first became evident in late pregnancy that the severe cervical dystocias occur. Patients 1 and 2 above fall into this category. Not knowing which patients will retain prolapse throughout the pregnancy, and having had such good results in our treatment, we feel that in spite of the time of occurrence of the prolapse, all patients who fall into this group may be treated alike and all will respond well. There is not much question that patients with pre-existing prolapse will need surgical relief after the pregnancy and puerperal involution periods are completed, but in the patient in whom prolapse occurs rather late in pregnancy there is hope that this form of treatment may bring about an alleviation of the prolapsed condition. At any rate, we feel that all patients are relieved during the pregnancy and that the labors of these patients can be made less arduous by the application of our method of treatment.

In previously reported cases, treatments have varied from the early suggestion of Findley[3] that therapeutic abortion and vaginal plastic be employed, to the idea propounded by Keettel[2] that the patient be delivered by means of Dührssen's incision and forceps or even further to the treatment by Porro cesarean section recommended by Harris.[4] The standard textbooks of obstetrics make no better suggestions, since Stander[5] recommends cervical incisions for dystocia and therapeutic abortion for incarcerated prolapsed pregnant uterus. In the group of 170 patients reviewed by Kibel,[1] the entire gamut of treatments were employed (Table I). In this group, the maternal mortality was 6.3 per cent, while the infant mortality was 22.1 per cent. Such statistics are very alarming but can be understood when one considers the picture that a pregnant prolapsed cervix presents. The organ is elongated, edematous, purplish red in color, and is friable and bleeds very readily on touch. Because of this, infection can take place rather easily and adding to such a situation an operative delivery would greatly increase the chances for sepsis. Stander reports such cases of maternal death from infection, and the deaths reported by Kibel were mostly the result of puerperal sepsis. Therefore, it would seem to us, any form of treatment that allows for spontaneous delivery is to be desired over any operative form of delivery.

TABLE I. METHOD OF DELIVERY IN 170 CASES OF PROLAPSE AND PREGNANCY REVIEWED BY KIBEL

METHOD	PER CENT
Spontaneous	34.7
Forceps	23.1
Dührssen's incisions	29.3
Version and extraction	4.3
Craniotomy	7.8
Porro-cesarean	0.8
	100.0

Treatment

As soon as the prolapse becomes evident, or as soon as a patient with prolapse becomes pregnant, the uterus is returned to normal position manually, and a Smith-Hodge type pessary of the proper size is inserted. This supports the uterus in the pelvis, prevents it from descending and, for the period of its use, ostensibly cures the prolapse. With the uterus held in place by the pessary, the patient may be up and about her usual business with no discomfort and without the dangers that might face her with the cervix protruding from the introitus. The use of the pessary in pregnancy is by no means a new procedure, but, in the past, as soon as a patient with a prolapsed pregnant uterus had uterine growth sufficient to pull the uterus into the abdomen and the cervix up into the vagina, the pessary was removed. If the prolapse again became evident, the patient was put to bed and kept there for the duration of the pregnancy because the bogey of obstetrics taught that a foreign body (pessary) in the vagina as term approached was a very dangerous thing. So, even though obstetricians may be advocates of early ambulation post partum, they will keep an otherwise healthy pregnant woman in bed throughout months of her pregnancy because of a simple prolapse which can be easily controlled. We do not remove the pessary, except for cleansing at regular

intervals, until the patient is in labor. When labor has begun to progress, effacement has taken place, and dilatation has proceeded to the point where 6 to 7 cm. of opening has been accomplished, the pessary is removed under sterile vaginal examination precautions. The pessary is cleansed and placed in cold sterilization for subsequent use. Labor has now progressed to the point where the danger of soft-tissue dystocia from the cervix no longer exists because retraction has taken place and the small amount of dilatation necessary to reach completion is easily and quickly accomplished.

When labor is completed and all lacerations and incisions are repaired, the pessary is removed from the sterilizing solution and reinserted. We consider this part of the procedure the most important one and the most radical departure from previously described techniques. It is to this part of the treatment that we ascribe our successful outcomes in Cases 1 and 2 where there were no prolapse conditions present after the involution periods were completed. The success of this therapeutic agent is obtained because the pessary keeps the uterus in proper position for adequate drainage and encourages proper uterine involution. The postpartum use of the pessary also takes the strain off the pelvic supporting structures and allows involution of these structures to take place to as great an extent as is possible. Anticipating questions of introduction of infection by the use of the pessary during pregnancy and in the puerperal period we can only say we have seen no such infection, we can see no reason to expect such infection, and we have no fear of infection.

Conclusions

1. Pregnancy superimposed on prolapse of the uterus and prolapse of the uterus occurring during pregnancy are uncommon combinations of conditions for which no previous adequate standardized treatment has been recommended.

2. Four cases of prolapse of the uterus and pregnancy are presented.

3. Treatment of this combination of conditions by use of a vaginal pessary during pregnancy, the first two-thirds of the first stage of labor and the puerperium is recommended.

4. This treatment has proved successful and presents no contraindications.

References

1. Kibel, I.: Am. J. Obst. & Gynec. **47**: 703, 1944.
2. Keettel, W. C.: Am. J. Obst. & Gynec. **42**: 121, 1941.
3. Findley, P.: J. A. M. A. **57**: 2131, 1911.
4. Harris, J. C.: J. South Carolina M. A. **8**: 248, 1912.
5. Stander, H. J.: Williams Obstetrics, ed. 8, New York, 1941, D. Appleton-Century Co

30 North Michigan Avenue

Discussion

DR. LESTER E. FRANKENTHAL.—I would like to take issue with the essayists as far as their four case reports are concerned. In Case 1, three months post partum there was no evidence of prolapse of either the cervix or the uterus. Case 2 falls into the same category. Case 3 showed evidence of prolapse post partum and was corrected by means of some surgical procedure. Case 4 presented an incarcerated retroverted uterus during pregnancy. However, puerperally, if I remember correctly, there was no evidence of prolapse. Therefore, I feel that three out of the four are not true cases of prolapse of the uterus. They fall into the category of hypertrophied, edematous, elongated cervices, a condition which is not infrequently seen during pregnancy and labor in the multipara.

Second, the essayists state that the descensus is aggravated by pregnancy. I fail to see where they have adequate proof of this conclusion. At approximately the fourth month of pregnancy the size of the corpus holds the uterus up out of the pelvis and unless there is an edematous cervix there will be no difficulty. As far as the use of a pessary post partum is concerned, the essayists claim that by the use of the pessary the uterus is kept in the proper position, allowing free and adequate drainage from the uterine cavity and likewise allowing the torn vaginal structures to regain their normal tonus. As far as the first part is concerned, I am heartily in accord. As far as the second part is concerned, if the cardinal ligaments, the pubocervical fascia, and the parametrium have been torn by a previous pregnancy, I fail to see how keeping the uterus in an anteverted position is going to allow restoration of these lacerated structures. If such were the case, I should think that the logical conclusion would be that if we had a first- or second-degree prolapse the introduction of a pessary, holding the uterus in the proper position for a period of a few months would suffice to correct the prolapse and removal of the pessary would find a normal genital status. Such is not the case.

From a statistical standpoint I would like to quote some statistics from Michael Reese Maternity Hospital. From Jan. 1, 1942, to date there were approximately 18,000 women delivered. During this time we have had three patients in whom the cervix protruded through the vulvar orifice. In two of these cases, postpartum check-up showed the genital tract to be normal; in other words, the edema and hypertrophy of the cervix had disappeared and there was no longer any problem. In one case, there was still a prolapse and this was treated by a Manchester operation. At the Maternity Center since July 1, 1932, there have been approximately 35,000 deliveries, of which 29,500, or 83 per cent were multiparas. In this number there were 11 women whose cervices protruded through the vulvar orifice; in other words, an incidence of one in 3,200 in the total series or 1 in 2,700 in multiparas.

As far as the treatment of labor is concerned, I do not feel that it requires any special comment. All of these patients had essentially normal deliveries. At Michael Reese Hospital, with the exception of one, all were normal spontaneous vaginal deliveries without complications in the puerperium. One case at the Maternity Center was terminated by means of version and extraction. In none of these cases was there any dystocia due to the edematous cervix or descent of the cervix.

DR. EDWARD L. CORNELL.—I want to warn the younger men not to be too critical of the practicing physician on the question of protrusion of the cervix or elongation of the cervix without protrusion. The practicing physician is not necessarily at fault. I have seen one case occurring in a primipara who came to me about the second month of pregnancy with a beginning prolapse or elongation of the cervix, whichever you wish to call it. The condition gradually became worse. A pessary was used and finally removed when the patient was about five months pregnant and the uterus remained up. It was a relatively easy delivery. She became pregnant again and approximately the same procedure was followed in the second pregnancy. In the interval between the two pregnancies the patient had no prolapse and no evidence of prolapse and no pessary was used post partum. She was allowed to stay in bed twelve or fifteen days, allowed up, and at the postpartum examination we found some descensus but nothing outside the vagina. I have never seen four multiparas with descensus but I am sure that such cases must occur. They can occur with and without the assistance of the physician.

DR. J. P. GREENHILL.—The matter of definition is important. Dr. Frankenthal is correct when he insists we should differentiate between a cervix which is outside the vulva and a real prolapse of the entire uterus. I fully agree that no matter what degree of prolapse there is, in nearly all cases, if pregnancy occurs, the uterus grows up out of the pelvic cavity into the abdomen, but the cervix may protrude out of the vagina. I have never seen a prolapse of the entire uterus which contained a pregnancy outside of the vulva. This condition is a true case of a prolapsed, pregnant uterus. In most cases where the cervix is at or outside the vulva, we are dealing with hypertrophied cervix and not a true prolapse. The cervix

is a remarkable structure. Many years ago Dr. DeLee and I each had almost duplicate cases of unusual hypertrophy of the cervix in nonpregnant uteri. We amputated the cervix in each case, but in a few years the cervices were again markedly hypertrophied.

In the only two cases of hypertrophy and prolapse of the cervix of a pregnant uterus I have seen, I had no trouble in delivering the patients. I see no objection to the use of a vaginal pessary during pregnancy.

Some of the statistics quoted by the authors are rather old and the prognosis for cases of prolapse of the cervix was poor. In the present state of our knowledge, infection is less important as a hazard than it was in former years.

DR. KLAWANS (Closing).—Dr. Frankenthal it seemed to me misunderstood or misquoted the paper. He apparently feels that unless he or some one close to him examines the patient the prolapse is not recognized. I think the doctors who examined these patients were able to differentiate. My understanding is that in practically every real case of descensus there is an elongated cervix, but when I stated in the paper that the cervix protruded three inches and that the lower uterine segment was lying on the perineum, that I should think would constitute a prolapse. Dr. Frankenthal did not read my statement that I did not expect a result in patients who had previous prolapse. Those patients would probably need surgery but we would save them trouble during labor and discomforts during pregnancy. Dr. Frankenthal stressed tearing of the supporting ligaments, I mentioned no such thing. I quote from the paper: "The postpartum use of the pessary also takes the strain off the pelvic supporting structures and allows involution of these structures to take place." I did not say they went back to normal. Dr. Frankenthal misquoted that. In his statistics from Michael Reese Hospital and from the Maternity Center there is no mention made of when in pregnancy these prolapses were seen, nor was mention made as to whether there was any treatment given. There is no differentiation between prolapses or elongated and hypertrophied cervices. We reserve the privilege of thinking that these patients we reported had true uterine prolapse.

To Dr. Greenhill, the last paper that I reviewed in which Dührssen's incision was advocated to facilitate delivery was written in 1941. That was relatively recent enough to be considered as modern.

UNSUSPECTED CERVICAL CANCER IN GYNECOLOGICAL PATIENTS

HAROLD SPEERT, M.D., NEW YORK, N. Y.

(From the Gynecological Service of The Roosevelt Hospital)

FEW experiences are more embarrassing to a gynecologist than the receipt of an unexpected pathological report of cervical carcinoma following operation for another condition. Such an occurrence, unfortunately, is not rare.

Bowers (1940), Diddle (1942), Graffagnino and McFetridge (1946), and Munnell (1947) have reported several cases in which carcinoma of the cervix was discovered for the first time by the pathologist after total hysterectomy. Three clinically unsuspected cases of cervical cancer in which the tumor was found incidental to plastic operations were recorded recently by Rubin (1945). Thirty-four per cent of the carcinomas of the cervical stump at the Sloane Hospital were discovered within 2 years following subtotal hysterectomy (Knight, 1943); and von Graff (1934), in a review of 581 published cases of stump cancer, found that symptoms of the tumor appeared within a year of operation in 23.5 per cent. In view of the slow growth of cervical carcinoma in its early stages, it is practically certain that most of these tumors were present but unsuspected at the original operation. Given (1947) observed that one-fourth of the stump cancers at the New York Hospital were discovered immediately after subtotal hysterectomy.

At the Roosevelt Hospital, carcinoma of the cervix has been diagnosed in fourteen cases in which there is no recorded preoperative suspicion of such a tumor. This represents a little over 2 per cent of all the cervical cancers. In most instances, the original operation was probably ill advised and would not have been done had the diagnosis been made beforehand. The recorded descriptions of the cervix suggest that in almost all the cases the tumor could have been detected by biopsy prior to operation. It is the purpose of this report to analyze these fourteen cases, to point out the diagnostic oversights, and to suggest methods for preventing their repetition.

The main features of each case are summarized in Table I. The patients varied in age from 30 to 58 years, the range in which most cervical cancers occur. In patients of this age group, the slightest indication of a cervical abnormality should arouse a suspicion of carcinoma and require that it be ruled out. In five cases, the cervical lesion was discovered in the routine examination of total hysterectomy specimens. Four of these operations were done for myomas, one for adenomyosis. In eight instances, the tumor was found in tissue removed incidental to plastic operations. Seven of these included trachelorrhaphies and one was a combined colporrhaphy preceded by routine curettage, the cervical tumor being discovered in the curettings. In one case, the cervical lesion was revealed in a postoperative biopsy after subtotal hysterectomy for fibroids.

Among the patients who underwent trachelorrhaphy, three also had abdominal uterine suspensions at the same operation, one including a myomectomy

TABLE I. UNSUSPECTED CERVICAL CARCINOMAS DISCOVERED AFTER OPERATION

CASE	YEAR	AGE	PREOPERATIVE DIAGNOSIS	OPERATION	CERVICAL CANCER	TREATMENT	REMARKS	FOLLOW-UP
1	1925	33	Myoma, retroversion, chronic cervicitis	D. & C., myomectomy, left salpingo-oophorectomy, suspension, trachelorrhaphy, colporrhaphy, appendectomy	Early	Radium, x-ray	No biopsy	Recurrence after 19½ years
2	1926	40	Lacerated and eroded cervix, vaginal relaxation, retroversion subinvolution	D. & C., cauterization, tracheloplasty, colporrhaphy, suspension, appendectomy	Grade 3	Hysterectomy, bilateral salpingo-oophorectomy, radium, x-ray	No biopsy	Well 2½ years
3	1928	40	Cystorectocele, prolapse	D. & C., trachelorrhaphy, colporrhaphy, interposition operation	Grade 2	X-ray, radium	Carcinoma concealed in canal	Well 12 years
4	1928	48	Cystorectocele, chronic cervicitis, retroversion	D. & C., trachelorrhaphy, colporrhaphy, interposition operation	Early	Radium, x-ray	No biopsy	Well 11 years
5	1930	56	Cystorectocele, prolapse	D. & C., trachelorrhaphy, colporrhaphy, suspension, right oophorectomy	Grade 1	Radium, x-ray	No biopsy	Well 14 years
6	1935	39	Adenomyosis, chronic cervicitis, metrorrhagia	D. & C., trachelorrhaphy, subtotal hysterectomy, bilateral salpingo-oophorectomy	Grade 3	Radium, x-ray	Carcinoma missed in preoperative curettings	Died 1½ years

7	1936	44	Myomas	Subtotal hysterectomy	Grade 3	Radium, x-ray	Cervix biopsied postoperatively	------
8	1939	39	Myomas, chronic cervicitis, metrorrhagia	Hysterectomy, bilateral salpingo-oophorectomy	Grade 1	X-ray	No biopsy	Well 1½ years
9	1939	36	Myomas, laceration cervix, chronic cervicitis, metrorrhagia	Trachelorrhaphy, subtotal hysterectomy, bilateral salpingo-oophorectomy, appendectomy	Grade 2	X-ray, radium	No biopsy	Well 7 years
10	1939	30	Lacerated cervix, chronic cervicitis, metrorrhagia	D. & C., trachelorrhaphy, Manchester operation	Grade 2	X-ray, radium	No biopsy	------
11	1942	41	Myomas, menometrorrhagia	Hysterectomy, bilateral salpingo-oophorectomy, appendectomy	"Carcinoma in situ"	None	No biopsy	Died of stomach carcinoma 4½ years later
12	1944	50	Myomas, chronic cervicitis, metrorrhagia	Hysterectomy, bilateral salpingo-oophorectomy	Grade 3	X-ray	No biopsy	Well 2½ years
13	1946	44	Cystorectocele, chronic cervicitis, prolapse	Trachelorrhaphy, colporrhaphy	Very early	Radical hysterectomy, bilateral salpingo-oophorectomy	Carcinoma missed in biopsy	Well 1 year
14	1947	58	Cystocele, cystitis, prolapse	D. & C., colporrhaphy, Manchester operation	Grade 2	Radium	History misleading carcinoma in canal	------

and salpingo-oophorectomy in addition. In two other cases, Watkins interposition operations were done. When the hysterectomy cases were reviewed, it seemed clear that at least three of the operations were performed for symptoms probably related to the unsuspected cervical cancer rather than to the recorded indication. Perhaps the most significant observation in this study is that in only one case was preoperative biopsy of the cervix done.

The choice of operations by which these patients were treated originally is beyond the scope of the present discussion. It should be noted, however, that the cases date back over more than two decades, during which time fashions in gynecological procedures have undergone change. For example, the combination of tracheloplasty and subtotal hysterectomy, once in common vogue, has been replaced largely by total hysterectomy. To an even greater extent, perhaps, have interposition operations been superseded by vaginal hysterectomy and the Manchester-Fothergill procedure.

The following 4 cases have been selected for individual analysis in the hope that the errors they embody may be of value to others.

CASE 2.—A 40-year-old white woman with two children was referred to the hospital for gynoplastic operation three months after the birth of her last child. Her last menstrual period had begun six days prior to admission and lasted two days. The recorded examination described the perineum as relaxed; the cervix soft, eroded, and bleeding slightly, with a large tear in the anterior lip and several smaller tears in the posterior lip; the fundus retroverted, enlarged, and softened. The preoperative diagnosis was laceration and erosion of cervix, cystocele, rectocele, lacerated perineum, retroversion and subinvolution of uterus. Operation the day after admission consisted of dilatation and curettage, anterior and posterior colporrhaphy, trachelorrhaphy, cauterization of cervix, round ligament suspension of uterus (Simpson), and appendectomy. In the process of curettage, the posterior wall of the uterus was accidentally perforated. Pathological report on the excised cervical tissue was epidermoid carcinoma. Twelve days later total hysterectomy and bilateral salpingo-oophorectomy were performed. The patient was given postoperative irradiation and was well two and one-half years later, when she was last seen.

Comment.—This patient's cervix received inadequate preoperative attention, in the mistaken belief that all the pathological alterations in it were the result of recent parturition.

CASE 9.—A 36-year-old Negro woman with two children complained of postmenstrual pain in the right lower quadrant of the abdomen. For the past three months she had noticed slight bleeding after coitus and a thin bloody vaginal discharge several days after each menstrual period. Her cervix was lacerated, eroded, and cystic, and bled easily on touch. The fundus was retroverted and contained a small nodule on its posterior surface. Operation consisted of trachelorrhaphy followed by subtotal abdominal hysterectomy, bilateral salpingo-oophorectomy, and appendectomy. At laparotomy, small myomas and chronic salpingitis were found. Pathological report on the excised cervical tissue was epidermoid carcinoma, plexiform type, grade 2. Postoperatively, the patient received a course of deep x-ray therapy to the pelvis followed by two applications of radium to the cervical stump for a total dose of 2,125 mg. hr. Seven years later she was well with no evidence of tumor recurrence.

Comment.—Preoperative biopsy of the cervix was indicated in this case by the history of postcoital bleeding, metrorrhagia, and the recorded description of the cervix.

CASE 11.—A 41-year-old nullipara began to have profuse, frequent, and irregular menstrual flow, often with clots and cramps, a year and a half before admission. She complained also of a heavy feeling in her pelvis. Her uterus was irregularly enlarged to the level of the umbilicus. The cervix was described as large, round, and smooth. Total hysterectomy, bilateral salpingo-oophorectomy, and appendectomy were performed. On pathological examination, in addition to a fibroid uterus, an irregular area of reddish discoloration and surface erosion measuring 7 mm. in diameter was described at the external cervical os. Microscopically, this

was diagnosed as "carcinoma in situ."* The patient remained well until almost four years and five months later, when she was readmitted because of abdominal pain of three months' duration. At operation she was found to have generalized abdominal carcinomatosis with ascites, but biopsy of a mesenteric implant was inadequate to establish the primary site of the tumor. The patient died twelve days later, autopsy disclosing an adenocarcinoma of the stomach with rupture and peritonitis. Careful examination of the pelvis failed to reveal any evidence of residual cervical cancer. The pelvic lymph nodes were free of tumor.

Comment.—Although it had no bearing on the ultimate outcome of the case, this patient's cervical lesion might have been discovered by more careful preoperative examination and biopsy.

CASE 14.—A 58-year-old white woman whose menopause had occurred 6 years previously complained of urinary frequency and recurrent attacks of "bleeding from the bladder" during the past year. She was believed to be suffering from hemorrhagic cystitis, and since a moderate cystocele and rectocele were present operative correction was decided upon, in the hope that this might help cure the urinary condition. The cervix was slightly prolapsed in the vagina but the mucosa appeared normal. The fundus and adnexa were atrophic. The urine contained many bacteria and a few leucocytes but no red blood cells. Operation consisted of dilatation and curettage, anterior and posterior colporrhaphy, and a modified Manchester procedure. The curettings, which amounted to only a few tiny fragments, showed epidermoid carcinoma of the cervix, grade 2. Five days postoperatively a 50 mg. capsule of radium was inserted into the cervical canal for sixty hours. Great difficulty was experienced in obtaining adequate exposure, and finally a considerable part of the plastic repair had to be undone before the radium could be inserted.

Comment.—This patient gave a misleading history. Her bleeding, which she later admitted to be from the vagina, resulted from an unsuspected and invisible endocervical carcinoma. Tumors in this location usually can be detected by curettage. The occasional discovery of unsuspected cervical carcinomas and asymptomatic endometrial neoplasms by the simple expedient of curettage recommends this procedure as a routine preliminary to all vaginal plastic operations in which the uterus is to be retained.

Discussion

The brightest prospect for improving the results in the treatment of cervical carcinoma lies in the early detection of cases. Early cervical cancers are discovered in proportion to the frequency with which they are suspected and the diligence with which they are sought. Schiller (1933) reported a 50 per cent reduction in the incidence of undiagnosed carcinoma by meticulous examination of the cervix preoperatively. In several clinics vaginal smears are now used routinely for this purpose, and in a few others all cervices are biopsied prior to major gynecological operations. Cervical biopsy is so simple and innocuous a procedure that it should be extended to every woman in whom there is the slightest suspicion of a cervical abnormality. A hundred negative biopsies are a small price for the discovery of a single early cervical cancer. It is the early, least suspected cases that are the most readily cured.

It has been common practice in the past, in this and other clinics, to treat various types of pathological cervices by tracheloplastic operation, doing any necessary vaginal plastic work at the same time. If the excised cervical tissue revealed carcinoma, as it did in seven cases in the present series, further treatment in the form of hysterectomy or irradiation was given. But in a few instances subtotal hysterectomy, uterine suspensions, or interposition operations were also done at the original sitting, without benefit of the pathological report

*When additional sections of the cervix were cut later a distinct area of invasion was found.

on the cervix. In these cases treatment of the cancer has been compromised, either necessitating another laparotomy or making radiation therapy more difficult, more hazardous, and less effective. A more rational method of approach to diseased cervices would seem to lie in preoperative biopsy before proceeding with major surgical treatment.

That the end results of treatment in this series of cases had not been consistently jeopardized, however, is suggested by the fact that at least five of the fourteen patients remained well for more than five years, and in only two cases was recurrence of the cervical tumor observed. This compares satisfactorily with the good prognosis usually associated with early cervical cancer.

Summary

1. Fourteen cases of unsuspected cervical carcinoma are reported which were discovered postoperatively by routine pathological examination or postoperative biopsy. Approximately 2 per cent of all cervical cancers were discovered in this manner.

2. Meticulous examination of the cervix with biopsy of suspect areas should precede all major gynecological operations.

3. Because of the occasional unsuspected endocervical and endometrial cancer which it brings to light, routine curettage is a worth-while preliminary to vaginal plastic operations.

References

1. Bowers, D. D.: Am. J. Obst. & Gynec. **39**: 830-836, 1940.
2. Diddle, A. W.: West. J. Surg. **50**: 449-451, 1942.
3. Given, W. P.: Am. J. Obst. & Gynec. **53**: 947-956, 1947.
4. von Graff, E.: Am. J. Obst. & Gynec. **28**: 18-31, 1934.
5. Graffagnino, P., and McFetridge, E. M.: New Orleans M. & S. J. **98**: 351-359, 1946.
6. Knight, R. v. D.: Am J. Obst. & Gynec. **46**: 333-349, 1943.
7. Munnell, E. W.: Am. J. Obst. & Gynec. **54**: 31-39, 1947.
8. Rubin, I. C.: J. Mt. Sinai Hosp. **12**: 607-615, 1945.
9. Schiller, W.: Surg., Gynec. & Obst. **56**: 210-222, 1933.

Addendum

Since this paper was written, publications by the following authors have mentioned several additional cases in which cervical cancer was discovered for the first time following major gynecological operations for unrelated conditions:

Diddle, A. W., and Bennett, T. R.: Am. J. Obst. & Gynec. **55**: 669-674, 1948.
Johnson, W. O.: Am. J. Obst. & Gynec. **56**: 100-109, 1948.
Brady, L.: Am. J. Obst. & Gynec. **56**: 939-943, 1948.

RESULTS IN 138 CASES OF ENDOMETRIOSIS TREATED BY CONSERVATIVE SURGERY

W. Benjamin Bacon, M.D., Boston, Mass.

(From the Free Hospital for Women, Brookline, Mass., and the Department of Gynecology, Harvard Medical School)

IN ENDOMETRIOSIS of sufficient degree to warrant laparotomy, a major problem is whether or not to conserve menstrual function and childbearing ability. While this must be decided for each patient as an individual by the sum of all the factors bearing upon her particular case, it was felt that an evaluation of two questions might be of assistance to the surgeon in this problem. If a conservative operation is performed, first, what are the chances for relief of symptoms or for progression or recurrence of the disease demanding later radical surgery or radiation; and, second, what is the outlook for future pregnancy? Table I, obtained from a review of the literature, summarizes the results of surgery in which the childbearing function was preserved.

Table I. Results From the Literature

Author	Year	No. of cases	(Expressed in per cent)			No. married and under 40	No. had children
			Cured	Improved	Failure		
Wharton[1]	1929	4	75		25	4	3
Read and Rogues[2]	1929	21	71.5	19.2	9.3		
Smith[3]	1929	40		32.5	0	?	2 per cent pregnant
Keene and Kimbrough[4]	1930	21	95.3	4.7	0	14	28 per cent normal pregnant
Cattell and Swinton[5]	1936	21	90	10	0	?	3
Pemberton[6]	1937	107			29	76	15
Counseller[7]	1938	98	56.2	19.8	24.0	55	6
Payne[8]	1940	{48	67	26	7	?	21
		{25	72	20	8	?	12
Fallas and Rosenblum[9]	1940	34	58.8	35.3	5.9	?	1 known child
Dannreuther[10]	1941	18	88.8	11.2	0	14	2
Holmes[11]	1942	24	29.1	54.1	16.6	?	12.6 per cent
Beecham[12]	1946	32			6.25	?	2 children 1 "preg. now"

Material

Two hundred fourteen cases of endometriosis treated by conservative surgery in the Free Hospital for Women and its private wing, the Parkway Hospital, from 1905 to 1941 inclusive, are reviewed. The data obtained from the hospital records were supplemented by answers to a questionnaire letter. Fifty-seven cases were rejected because of insufficient follow-up studies. An additional 19 cases, including endometriosis of the cervix, vagina, abdominal scar, hernial

sac, umbilicus, and perineum were rejected as not constituting per se an indication for laparotomy, and, therefore, not bearing upon the question of conservative versus radical surgery. This report is concerned with the remaining 138 cases of intra-abdominal, pelvic endometriosis, diagnosed grossly and histologically, and treated by laparotomy at which the childbearing function was anatomically preserved.

Results

TABLE II. RELIEF OF SYMPTOMS

	NUMBER OF CASES	PER CENT
Relieved	68	49.3
Partially relieved	29	21.0
Failure	41	29.7

In Table II, the group of cases classed as "relieved" includes those patients who stated without question that they were relieved, together with those who were "improved" or "better," except for symptoms which were felt to be mild, and in whom pelvic examination was essentially negative. The group classed as "partially relieved" includes those who were, for the most part, helped by operation, but in whom a significant degree of symptoms remained or recurred. If there was any doubt as to a reasonably high degree of symptomatic relief, the case was classed as "partially relieved," rather than "relieved." No further treatment was given in the above two groups. The group classed as "failure" were those in whom continuance or recurrence of symptoms necessitated either radical surgery or radiation therapy.

Pregnancy Following Operation

One hundred twelve patients in the series were married and under 40 years of age; of these, 30, or 26.8 per cent, delivered a total of 39 living children. Twenty-three patients had one child each, six had two children, and one had four children. In addition to the above 30 patients, seven patients reported one miscarriage each. The time between operation and delivery ranged from 11 months to 6 years, the average interval being 2.7 years. Of the above thirty patients who had children, twenty-two were classed as being relieved of their symptoms, three as partially relieved, and five as failures.

The question, "Have you wanted to have children since operation?" was included in the questionnaire letter. While the answers to this question were too few to determine how many of the series as a whole wanted children, there were an appreciable number of answers in the negative. Thus it is possible that there were more potential children in the series than those recorded.

Later Treatment

Forty-one patients, or 29.7 per cent (those classed as "failure" in Table II), required further treatment; this is summarized in Table III.

TABLE III. LATER TREATMENT

Hysterectomy	26
Pelvic laparotomy (miscellaneous procedures)	5
Radium	4
X-ray	6

Pathologic diagnosis is available in twenty of the cases treated by hysterectomy; of these, only nine showed recurrent endometriosis. The findings in the remaining eleven cases include adhesions, chronic salpingitis and oophoritis,

retention cysts and fibroids (one case), but no endometriosis was demonstrable. These eleven cases, although symptomatically demanding reoperation, bear out the fact, at least from a pathologic standpoint, that the disease is not always progressive, which is a point in favor of conservatism. The time between the first and second operation ranged between 4 months and 14 years, the average interval being 4.8 years.

Correlations

An attempt is made in this review to ascertain whether any factors exist which might have a bearing upon the postoperative outcome of a case in respect to symptomatic relief and future pregnancy. In other words, are there any criteria that might enable the surgeon to determine which patients are more likely to be symptomatically relieved and become pregnant, after a conservative operation, and which cases are less likely to attain this desired result.

The factors which should be considered in regard to their possible bearing upon this result are age, symptomatology, and pathologic findings.

Age.—The age at the time of operation of the married patients in the series, and of the patients who subsequently delivered children, is given in Table IV.

TABLE IV. AGE INCIDENCE

YEARS (INCLUSIVE)	MARRIED PATIENTS 115 CASES	PATIENTS DELIVERING CHILDREN 30 CASES
19-24	14	7
25-29	35	12
30-35	48	11
36-39	15	-
40-46	3	-

It is true in general that the younger the patient, the better is the outlook for subsequent pregnancy. Table IV indicates that this statement also applies to this series.

The possible bearing of age upon the outlook for symptomatic relief was studied. The ages of the cases previously classed as "relieved," "partially relieved," or "failure," fell into essentially parallel age groups, from which it is inferred that no correlation between age and prognosis for symptomatic relief can be shown in this series.

Symptomatology.—The incidence of symptoms in the series elicited by history before operation is tabulated in the first column of Table V. The number of patients in each of the three groups, previously classed as "relieved," "partially relieved," or "failure," who complained of the particular symptom is tabulated in the remainder of Table V.

TABLE V. SYMPTOMATOLOGY

SYMPTOM	NO. OF CASES	NO. OF CASES IN EACH GROUP HAVING THE SYMPTOM					
		RELIEVED: 68 CASES		PARTIALLY RELIEVED: 29 CASES		FAILURE 41 CASES	
		NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Dysmenorrhea	75	35	51.4	11	37.9	29	70.7
Low abdominal pain	59	26	38 2	15	51.7	18	43.9
Backache	35	17	25.0	6	20.7	12	29.3
Abnormal bleeding	26	14	20.6	4	13.8	8	19.5
Sterility	18	12	17.6	4	13.8	2	4.9
Headache	14	6	8.8	2	6.9	6	14.6
Nausea, vomiting	9	7	10.3	1	3.5	1	2.4
Pelvic pain	8	5	7.4	1	3.5	2	4.9
Dyspareunia	7	5	7.4	0		2	4.9
Rectal pain	5	2	2.9	1	3.5	2	4.9
Bladder symptoms	3	1	1.5	1	3.5	1	2.4

It was felt that evaluation of the degree or severity of symptoms from written records would be invalid. Therefore Table V expresses only the comparative frequency with which each symptom occurred in each of the three above groups. It is seen that these symptoms appear in each group with the same relative frequency. Therefore, no prognosis of value can be derived from this study of symptomatology.

Pathologic Findings.—The pathologic findings in the series are classified as to location of endometriosis on the basis of (a) ovarian endometriosis (i.e., whether it is absent, unilateral, or bilateral) and (b) the presence or absence of the disease elsewhere in the pelvis. This divides the series into the five classes which are listed in the first column of Table VI. The operations by which these five classes were treated are also recorded. Thus, the location and extent of endometriosis are judged both by the operative findings and the magnitude of the operation necessary to relieve them. It is seen that the extent of the disease, and that of the corresponding operation, increases progressively from Class 1 to Class 5. This classification is made in an attempt to determine whether any significant difference in postoperative results exists between the cases with minimal endometriosis and a minor operative procedure at one extreme, and those with a considerable amount of the disease and a comparatively extensive operation at the other.

TABLE VI. PATHOLOGIC FINDINGS CORRELATED WITH SYMPTOMATIC RELIEF AND SUBSEQUENT PREGNANCY

LOCATION OF ENDOMETRIOSIS	OPERATION	NO. OF CASES	SYMPTOMATIC RELIEF (EXPRESSED IN PER CENT)			SUBSEQUENT PREGNANCY	
			RELIEVED	PARTIALLY RELIEVED	FAILURE	NO. OF CASES MARRIED AND OVER 40	PER CENT HAVING CHILDREN
1 Negative ovaries Pelvic E.*	Excision of E.	32	59.4	6.2	34.4	26	23.1
2 Unilateral ovarian E. negative pelvis	Resection ovary; or O* or SO*	61	41.0	29.5	29.5	49	24.5
3 Unilateral ovarian E. plus pelvic E.	Resection ovary and excision E.; or O or SO, and excision E.	22	63.6	13.6	22.8	19	36.8
4 Bilateral ovarian E. negative pelvis	Resection both ovaries; or O or SO, and resection other ovary	11	36.3	18.2	45.5	8	25.0
5 Bilateral ovarian E. plus pelvic E.	Resection both ovaries and excision E.; or O or SO, resection other ovary and excision of E.	12	50 0	33 3	16.7	10	30.0
Results in Series as a whole		138	49.3	21.0	29.7	112	26.8

*E – Endometriosis
O – Oophorectomy.
SO – Salpingo-oophorectomy.

Pelvic endometriosis includes involvement of the uterine serosa and supporting ligaments, anterior and posterior cul-de-sac, and elsewhere on the pelvic peritoneum. In the majority of cases it is believed to be slight or moderate, in that many cases show only a few minute implants or a small area with adhesions separated without difficulty. This is particularly true of pelvic endometriosis

in which the ovaries are negative. Dense adhesions and a large amount of endometriosis are more common in cases of ovarian involvement plus pelvic endometriosis. The bowel was not involved to a significant extent in any case.

One hundred six cases showed ovarian endometriosis; in twenty-three of these cases, this lesion was bilateral. The degree of ovarian involvement is indicated by the fact that resection of the lesion, with preservation of ovarian tissue on the affected side, was possible in 77 instances. In the remaining 52 instances, oophorectomy or salpingo-oophorectomy was performed. In the 52 cases in which the operation included either oophorectomy or salpingo-oophorectomy, the latter procedure was carried out 32 times, which indicates the frequency of tubal involvement. In this connection, there were two cases of ruptured tubal pregnancy in which endometriosis was an incidental finding. The gross diagnosis at operation of ovarian (unilateral or bilateral) and pelvic endometriosis was confirmed histologically in all but seven lesions. These were small implants treated by fulguration.

The operative procedures listed in Table VI were combined with suspension of the uterus in all but 8 cases. Incidental appendectomy was performed in 33 cases. Anterior colporrhaphy, perineorrhaphy, and herniorrhaphy (inguinal, femoral, and incisional) were included in a few cases. Presacral neurectomy was performed in 19 cases; of these, 13 were relieved of symptoms, three partially relieved and three were failures. There was no operative mortality in the series.

The results in symptomatic relief and subsequent pregnancy are recorded for each of the five classes in the series (Table VI). No significant difference can be shown in these results between those with minimal endometriosis and a minor operative procedure at one extreme, and those with a considerable amount of the disease and a comparatively extensive procedure at the other. The cases showing negative ovaries and pelvic endometriosis (Class I) had in many instances only a few small implants and no adhesions. The results in this class are not significantly different from the results in the series as a whole, in that, while approximately 10 per cent more cases were relieved, there were 5 per cent more failures and 3 per cent less pregnancies. The results in the 23 cases of bilateral ovarian endometriosis (Classes 4 and 5 combined) are as follows: Relieved 43.5 per cent, partial relief 26.4 per cent, failure 30.1 per cent, subsequent pregnancy 27.8 per cent. These results are essentially the same as those in the series as a whole. The results in the twelve cases showing the greatest amount of endometriosis in the series (Class 5) are slightly better than the results in the series as a whole.

Thus, no correlation can be shown between the amount and location of endometriosis and postoperative symptomatic relief and future pregnancy. One might infer, however, that the presence of a considerable amount of endometriosis is not a contraindication, from the point of view of prognosis, to a conservative operation.

Summary

1. One hundred thirty-eight cases of pelvic endometriosis, treated by laparotomy which conserved childbearing ability, are reviewed.

2. Sixty-eight of these cases, or 49.3 per cent, were relieved of symptoms; 29, or 21 per cent, were partially relieved; and 41, or 29.7 per cent, were failures, requiring later radical surgery or radiation.

3. One hundred twelve patients in the series were married and under 40 years of age; of these, 30, or 26.8 per cent, delivered a total of 39 living children. The average interval between operation and delivery was 2.7 years.

4. The prognosis for symptomatic relief and future pregnancy does not seem to be affected by age, symptomatology, the location and extent of the disease, or the magnitude of the conservative operation performed.

Conclusion

A conservative procedure can be recommended, even in the presence of a considerable amount of endometriosis.

The author wishes to thank Drs. George Van S. Smith and Arthur T. Hertig for their help in the preparation of this paper, and Dr. George W. Corner, Jr., for his review of pathologic material.

References

1. Wharton, L. R.: South. M. J. **22**: 267-271, 1929.
2. Read, C. D., and Rogues, F.: Brit. M. J. **1**: 1159-1160, 1929.
3. Smith, G. V. S.: Am. J. Obst. & Gynec. **17**: 806-814, 1929.
4. Keene, F. E., and Kimbrough, R. A.: J. A. M. A. **95**: 1164-1168, 1930.
5. Cattell, R. B., and Swinton, N. W.: New England J. Med. **214**: 341-346, 1936.
6. Pemberton, F. A.: New England J. Med. **217**: 1-5, 1937.
7. Counseller, V. S.: Am. J. Obst. & Gynec. **36**: 877-888, 1938.
8. Payne, F. L.: Am. J. Obst. & Gynec. **39**: 373-382, 1940.
9. Fallas, R., and Rosenblum, G.: Am. J. Obst. & Gynec. **39**: 964-975, 1940.
10. Dannreuther, W. T.: Am. J. Obst. & Gynec **41**: 461-474, 1941.
11. Holmes, W. R.: Am. J. Obst. & Gynec. **43**: 255-266, 1942.
12. Beecham, C. T.: Am. J. Obst. & Gynec. **52**: 707-718, 1946.

SUSPENSION AND THE RETROFLEXED UTERUS

A Review of Cases

I. A. PERLIN, M.D., C.M., HALIFAX, NOVA SCOTIA

(From the Department of Obstetrics and Gynaecology, Dalhousie University)

FOR some time there has been, in this Department, a great deal of skepticism concerning the value of suspension operations performed to alleviate symptoms which are supposedly due to retroflexed uteri. As a result, a review was made of all cases of retroflexed uteri for which suspensions were performed in this Department during the years 1925 to 1946, the majority, of course, because of the above skepticism, having been done in the earlier years.

A total of 93 cases was accumulated. This figure represents all of the cases on which complete records were available, and all were operated upon in the Victoria General Hospital, Halifax, Nova Scotia, by the members of this Department only, who, therefore, had similar technique and standards. Follow-up letters were sent and the questionnaire was essentially of this nature (no leading questions asked).

1. Did the operation on_____ (date) cure your symptoms (enumerated)?
   Yes? No? If so, for how long?
2. Did you have any children since operation?
   Yes? No? How long after operation was first one?
3. Did you have any miscarriages since operation?
   Yes? No? How long after operation was first one?

From these 93 cases, 44 replies were received. Three women had died during the interval, seven did not reply even after a second request and 39 letters were returned from the dead letter office. Those who did not reply (7) constituted such a small number that their answers could hardly have influenced the results to any significant degree even if they had all been extreme results at one end of the scale or the other. The 39 letters from the dead letter office were due to "shift in population," and not to failure to reply, so one can be safe in assuming that these would have been no worse or no better than the sample from whom reports were received. So that, of the total number, contact was established with all cases possible, and the 44 from whom replies were received represented the various years from 1925 to 1946 and were, therefore, a good indication of what the average results must be.

Conditions at Time of Operation

TABLE I. AGE OF PATIENTS

AGE IN YEARS	NO. OF PATIENTS
18 to 30	28
31 to 40	10
41 to 50	4
Over 50	2

It should be noted that the two patients over 50 years of age had retroflexed uteri associated with prolapse and the suspension was done in addition to repair. This was during the earlier years, when such a combined operation was in vogue. This combined operation is not done now in our department.

TABLE II. PREVIOUS PREGNANCIES

PREGNANCIES	NO. OF PATIENTS
0	9 (2 unmarried)
1 to 3	25
4 to 8	10

TABLE III. SYMPTOMS AT TIME OF OPERATION

SYMPTOMS	NO. OF CASES
Pain in iliac region or regions	29
Discharge per vaginam	21
Backache	15
Dysmenorrhea	10
Dyspareunia	4
Menorrhagia	3
Sterility	3

There is considerable overlapping (since the total does not add up to 44), but this is due to the fact that some cases had more than one symptom.

TABLE IV. ASSOCIATED CONDITIONS

CONDITIONS	NO. OF CASES
Cervical erosion	8
Cervicitis	4
Cervical laceration	5
Ovarian cyst (simple follicular)	2
Fibroids	2
Benign uterine bleeding	3
Cystocele	2
Relaxed perineum	2
Anxiety syndrome	1

Here again there is overlapping because some cases had more than one associated condition. (Total number with associated conditions 24.)

TABLE V. OPERATIONS PERFORMED (IN ADDITION TO THE 44 SUSPENSIONS)

OPERATIONS	NO. OF CASES
Cauterization of cervix	11
Repair of cervix	5
Oophorectomy	2
Enucleation of fibroids	2
Curettage	3
Perineorrhaphy	2
Presacral sympathectomy	3
Appendectomy	9

There were 24 patients who had operations in addition to suspensions so that the overlapping here is due to the fact that some had more than the two operations.

Results of Inquiry

A. *Cases of Uncomplicated Retroflexion.*—

There were 14 patients who had suspensions only and 6 cases in which an appendectomy was done in addition to the suspension (the appendix ap-

parently normal from the pathologic reports and removed only as a routine). Therefore, there were 20 cases of uncomplicated retroflexion and the results in these are tabulated in Table VI.

TABLE VI. RELIEF OF SYMPTOMS BY SUSPENSION ALONE

DEGREE OF RELIEF	NO. OF CASES	SYMPTOMS RELIEVED	SYMPTOMS NOT RELIEVED
Complete	7	Iliac pain, backache, dysmenorrhea, deep dyspareunia	—
Temporary*	2	Iliac pain, backache, discharge	All symptoms recurred after one to five years
Partial†	7	Iliac, pain, backache, discharge	Iliac pain, discharge, sterility, dysmenorrhea
None	4	—	Iliac pain, deep dyspareunia

*Temporary relief indicates complete relief of symptoms for 1 to 5 years.

†Partial relief indicates relief of some symptoms for from 6 months to present but no relief of other symptoms.

It can readily be seen that only 7 cases of the 20 (i.e., 35 per cent) had complete relief of all their symptoms while the remaining 13 (i.e., 65 per cent) had little or no relief. Further, there was no consistency as between which symptoms were relieved and which not.

B. *Remaining Results* (where other operations for definite lesions were performed in addition to the suspension).—

1. No. of cases with cervicitis and/or erosion in which, in addition to suspension, a cauterization was done - - - 10. Results tabulated in Table VII.

TABLE VII. SUSPENSION PLUS CAUTERIZATION OF CERVIX

DEGREE OF RELIEF	NO. OF CASES	SYMPTOMS RELIEVED	SYMPTOMS NOT RELIEVED
Complete	6	Iliac pain, backache, discharge, dysmenorrhea	—
Partial	1	Sterility	Dsymenorrhea
None	3	—	Iliac pain, discharge, dysmenorrhea

Here again there is a definite lack of consistency in the relief of symptoms with the exception of backache. But it is quite obvious that one cannot attribute the relief of backache to the suspension because the original cause may well have been the erosion or cervicitis and thus the backache was relieved by the cauterization.

2. Number of cases with laceration of cervix on which, in addition to suspension a trachelorrhaphy was done - - - 2
Partial relief - - - - - - - - - - - 2
Relief of some symptoms for 2 to 3 years: discharge, dysmenorrhea, iliac pain; but no relief of other symptoms: backache, iliac pain.

3. Number of cases associated with laceration of cervix and relaxed perineum on which both a trachelorrhaphy and perineorrhaphy were done in addition to suspension - - - - - - - 2
Complete relief - - - - - - - - - 2
Symptoms: backache, discharge.

In this group one cannot attribute the relief of symptoms to the suspension because the backache may well have been due to either or both the laceration and the relaxed perineum and the discharge due to the laceration, so that the trachelorrhaphy and perineorrhaphy may well have been the reason for the relief of the symptoms.

4. Number of patients with fibroids on whom enucleation was done in addition to suspension - - - - - - - 2
Complete relief - - - - - - - - - - 2
Symptoms: sterility, iliac pain.

Here, again, if we can rightly say that the operation cured the sterility, then we must remember that this symptom may well have been due to the fibroids and with their enucleation pregnancy supervened, rather than because of the suspension. It should be noted here that these patients became pregnant six to eight years following the operation so can one say it was due to either part of the operation?

5. Number of cases in which a curettage was done in addition to suspension - - - - - - - - - - - - - 2
Complete relief: menorrhagia - - - - - 1
Partial relief - - - - - - - - - - - 1
Relief of symptoms for 2 years: menorrhagia.
No relief of others: backache.

Here again, possibly the curettage, and not the suspension cured the menorrhagia.

6. Number of cases associated with marked dysmenorrhea and anxiety for which a presacral sympathectomy was done in addition to suspension - - - - - - - - - - - - - - 2
No relief - - - - - - - - - - - - - 2
Symptoms: discharge, dysmenorrhea, menorrhagia, iliac pain.

(In both cases nerve fibers were found in the material removed.)

7. Number of cases associated with ovarian cyst in which oophorectomy was done in addition to suspension - - 1
No relief - - - - - - - - - - - - 1
Symptoms: backache.

8. Number of cases associated with prolapse (cystocele) in which a repair was done in addition to suspension - 2
Complete relief - - - - - - - - - - 2
Symptoms: backache, discharge, iliac pain.

In this group the cystocele may well have caused these symptoms, and the relief obtained may have been due to the repair and not necessarily the suspension.

9. One patient had many operations in addition to suspension (appendectomy, oophorectomy, curettage, cauterization, presacral sympathectomy).
Complete relief - - - - - - - - - - 1
Symptoms: discharge, backache, menorrhagia, and iliac pain.

With this type of shotgun procedure any one of the operations could have relieved the complaints.

TABLE VIII. SUMMARY OF RELIEF OF SYMPTOMS IN SECTION B (WHERE OTHER OPERATIONS WERE PERFORMED IN ADDITION TO SUSPENSION FOR ASSOCIATED CONDITION)

DEGREE OF RELIEF	NO. OF CASES	SYMPTOMS RELIEVED	SYMPTOMS NOT RELIEVED
Complete	14	Iliac pain, backache, discharge, dysmenorrhea, sterility, menorrhagia	—
Partial*	4	Iliac pain, discharge, dysmenorrhea, menorrhagia, sterility	Iliac pain, backache, dysmenorrhea
None	6	—	Iliac pain, backache, discharge, dysmenorrhea, menorrhagia

*Partial relief indicates relief of some symptoms for from two years to present but no relief of other symptoms.

In this section, 14 cases (59 per cent) experienced complete alleviation of their symptoms while 10 cases (41 per cent) had little or no relief. This was not significantly better than the results in Section A, and, further, as has been pointed out above, the other operations performed in addition to the suspensions were probably responsible for the cure of many of the symptoms.

The number of complete cures in the foregoing series seems unrewardingly small. Furthermore, there was a marked lack of consistency in the relief of symptoms.

Our results also throw skepticism on the indications for suspension in uncomplicated retroflexion usually given in the textbooks, namely: habitual abortion, sterility, iliac pain, backache, and dysmenorrhea.

Habitual Abortion.—Of the 44 patients, only 2 gave a history of more than one abortion, both of these having had 5:

(a) The first one was a woman, aged 37 years, who had had one full pregnancy (thirteen years) and then five abortions before the suspension (the last one having been one year prior to the operation). Since the uterus was suspended (plus cauterization of cervix for cervicitis) patient has not been pregnant, seventeen years after operation.

(b) The second patient was a woman aged 32 years, who had had three full pregnancies (seven years to four years), and then five abortions in two years, prior to the operation. Since the suspension in 1935, patient has had three full pregnancies (the first one one year after operation), and then had two abortions since the full pregnancies to date. The net result seems to be similar to the condition before operation, although it would appear that the suspension might have relieved the situation for a short time.

So, in the only two cases of habitual abortion in our series, one had no proved relief, the other had only a partial, if any, degree of success.

Sterility.—In the case of sterility, only seven (married) of the 44 patients had not had children previous to the operation and of these only three had actually complained of the condition:

(a) One of these three had a simple retroflexed uterus and she has not become pregnant yet (10 years).

(b) The other two had associated fibroids which were enucleated. These became pregnant six to eight years postoperatively, respectively. In these cases one can surely not attribute the successful pregnancies to either the suspension or the enucleation of the fibroids.

Of the four patients who did not complain of sterility, only one has become pregnant to date, her first pregnancy having been one and one-half years after the operation. In this case, first, we are not sure how long she was married before the operation (she was 27 years old), and, second, it took a year and a half after the suspension before impregnation occurred. Surely, we cannot claim that the pregnancy in this case was due to the operation. Furthermore, I am informed by a member of our staff that he has done fourteen suspensions, where uncomplicated retroflexion was the only condition found as between husband and wife. In only one case did the patient become pregnant in a sufficiently short time to lay it to the operation, and that a woman who had previously had children.

Iliac Pain.—Of the 20 patients with uncomplicated retroflexion (in 6 of whom a routine appendectomy was done), 13 complained of iliac pain, of whom 8 obtained complete relief, 2 of these having had an appendectomy.

Backache.—Of the same 20 patients, 10 had backache, of whom 6 got complete relief.

Dysmenorrhea.—Of the same 20 patients, only 2 complained of this symptom, of whom one got relief.

The retroverted uterus has proved a constant source of surprise to us. This is the sort of thing by which we are nonplussed: A patient comes into our service who has been with us before. Some years ago we did a suspension for a retroverted uterus. She is now back for something altogether different. The suspension, she tells us, was a complete success and she has never had symptoms due to the retroversion since. Yet we find on examination that the uterus is back in the same position it was before we suspended it. Another woman on whom we have done a suspension gets complete relief of her symptoms for some years. But they recur. She is convinced that the retroversion has also recurred. So she is admitted to hospital prepared to have another suspension. We find on examination that the uterus is nicely anteverted. Here is another woman with symptoms suggesting a retroverted uterus. On examination she has a retroverted uterus. We do not operate on her. We see her several times and she still has the retroversion. Then another doctor sends her in again for operation, and we find that the uterus in the meantime has anteverted itself (but she still has all the symptoms). Another woman has a retroverted uterus that appears to be causing some symptoms. We insert a Hodge pessary after anteverting the uterus under anesthetic. She comes back in three months with all her symptoms gone, but as a result of family manipulations the pessary has got turned over on its side, the uterus has returned to its ancient retroversion. Or here is another woman who gets complete relief of her symptoms as a result of suspension until her husband leaves her, when they all recur, yet the uterus has remained anteverted. It is this sort of thing, coupled with the general results stated in this paper, that have led us to wonder if the retroverted uterus can justifiably be blamed for any symptom other than that type of deep dyspareunia where the ovary gets caught between the retroverted uterus and the banging penis.

Conclusion

We thus cannot say that, in our operative experience at the Victoria General Hospital, suspension has played a really satisfactory part in the cure of uncomplicated retroversions. The number of complete cures has been so small as to cause us to ask ourselves if the suspension in such cases did not act psychologically rather than somatically. Furthermore, the lack of consistency in the symptoms cured, or not cured, is so outrageous that we doubt the validity of blaming any of them on the retroverted uterus. In short, we are left in a state of complete skepticism with regard to the retroverted uterus as a producer of symptoms, and of suspension as a cure for such symptoms.

As a result of this we now do not do a suspension except under these conditions: (a) the uterus is anteverted, if necessary under Pentothal anesthetic, (b) a Hodge pessary is inserted and left in for three months, (c) the pessary is removed and left out for a month. If, as a result of the insertion of the pessary, the symptoms are relieved, and if they recur when the pessary is removed, we feel that the operation might be justified—but we have had it fail to cure even in cases where such precautions were taken. We believe, nevertheless, that the operation should never be done until the pessary has been used in the manner just indicated.

I am greatly indebted to Dr. H. B. Atlee, Chief of the Department of Obstetrics and Gynaecology, and to Dr. C. B. Stewart, Professor of Epidemiology, Dallhousie University, for their suggestions and advice in the preparation of this paper.

DICUMAROL IN THE TREATMENT OF ANTENATAL THROMBO-EMBOLIC DISEASE

Report of a Case With Hemorrhagic Manifestations in the Fetus

JULIUS J. SACHS, M.D., AND JOHN S. LABATE, M.D., NEW YORK, N. Y.

(From the Departments of Medicine and of Obstetrics and Gynecology, New York University College of Medicine, and the Third [New York University] Division, Bellevue Hospital)

THE use of dicumarol during the postpartum period has been established as a safe method of therapy for venous thrombosis, without inducing uterine bleeding.[1, 2] Barnes and Ervin[2] have used the drug prophylactically during labor with no untoward effect, and anticoagulant prothrombin levels were not reached until after delivery. Similar results have been obtained by Allen and his group[3] in the treatment of venous thrombosis and pulmonary embolism following delivery.

Because of the infrequency of antenatal thromboembolic disease, little is known of the effect of dicumarol on the human fetus. However, the earliest reports on sweet clover disease in cattle demonstrated the increased susceptibility of the new-born calf to this hemorrhage producing agent.[4, 5, 6] Schofield[4] described a calf, born of a cow fed spoiled sweet clover hay, that developed typical hemorrhagic symptoms within a few hours after birth and died, while the mother remained well. Roderick[5] noted that an active well-developed calf, born of a cow fed for thirteen days on damaged sweet clover, died of hemorrhage twenty-eight hours after birth. In a study on newborn pups of a pregnant dog given dicumarol before parturition, Quick[7] found that out of a litter of seven, the four pups not treated with vitamin K died of hemorrhage, whereas the pups that received vitamin K survived.

It would appear possible, as Quick[7] surmised, that similar hemorrhagic tendencies might appear in the human fetus following the antenatal use of dicumarol. The case which follows represents the first known experience at Bellevue Hospital of the hemorrhagic effect of dicumarol on the fetus of a mother receiving prolonged therapy with this drug for the control and treatment of thrombo-embolic disease.

Report of Case

O. S., a 23-year-old Puerto Rican multipara, was admitted to the emergency medical ward of Bellevue Hospital on July 25, 1947, during the seventh month of her pregnancy, in acute respiratory distress. Her illness began four days previously with the sudden onset of pleuritic pain in the left chest, and dyspnea. This was associated with cough and fever, but no hemoptysis. The thoracic pain continued, and the dyspnea became progressively more severe, finally requiring hospitalization.

Her two previous pregnancies in 1943 and 1944 were uneventful, except for the presence of an associated anemia. She denied any knowledge of heart disease. Her last menstrual period was December 23, 1946. During the few months preceding the present illness she had noted recurrent pains in both calves, the soles of both feet, and in the medial aspects of both thighs.

On admission, physical examination revealed an apprehensive, slender woman, who was extremely dyspneic and orthopneic. The respiratory rate was 52, the temperature was 101° F., the pulse rate was 138, and the blood pressure was 120/70. There was pallor of the skin and mucous membranes, but no icterus. The neck veins were not distended. The breasts were engorged. Both sides of the chest were filled with many coarse bubbling râles, extending from the apices to the bases, anteriorly and posteriorly. The apical impulse of the heart was in the fifth intercostal space, just inside the mid-clavicular line. There was a soft systolic murmur at the apex and at the pulmonic area. The uterus was enlarged to the size of a seven-month gestation. Fetal heart sounds were audible in the right lower quadrant. Examination of the extremities revealed marked bilateral calf-muscle tenderness along the course of the deep veins in the calves. There was tenderness in the adductor group of muscles of both thighs. Homans' sign was positive bilaterally.

Treatment was immediately started and consisted of oxygen by mask, bloodless phlebotomy, intravenous hypertonic sucrose, papaverine, and aminophylline. The patient responded favorably, and within an hour, the respiratory rate had returned to normal, and a few râles remained at both bases. She was not digitalized.

The urine was normal; the red blood count was 3,000,000 with a hemoglobin of 7.0 Gm. per cent; the white blood count was 9,200 with 65 per cent polymorphonuclear leucocytes, 6 per cent band metamyelocytes, 20 per cent lymphocytes, 6 per cent monocytes, 2 per cent eosinophiles and 1 per cent basophiles; mean corpuscular volume was 80 cu. microns; mean corpuscular hemoglobin was 23 micro-micrograms; mean corpuscular hemoglobin concentration was 29 per cent; the blood smears showed a hypochromia, nucleated red cells, and target cells; there was no increased fragility of the red cells to hypotonic saline; the sickling preparation was negative; stools were repeatedly negative for ova and parasites; the Mazzini test of the blood for syphilis was negative; blood type was O, Rh positive; the albumin-globulin ratio was 4.5/2.0; the icteric index was 5; the nonprotein nitrogen was 28 mg. per cent; the cephalin flocculation test was positive during pregnancy, but subsequently remained persistently negative. An x-ray of the chest, taken the day after admission, showed clear lung fields, and a heart that was normal in size and shape. The electrocardiogram was normal.

A diagnosis was made of bilateral phlebothrombosis of the deep veins of the leg with pulmonary embolism, and anticoagulant therapy was started. Heparin was given intravenously in 100 mg. doses every six hours for eight doses, and dicumarol was given orally in doses of 200 mg. for the first three days, and then in accordance with the prothrombin time, as shown in Figs. 1 and 2. The prothrombin time was determined by the Link-Shapiro modification[8]* of the Quick method.

The patient continued to have signs of deep vein thrombosis in the legs and thighs. However, examination of the chest remained negative. On the sixth hospital day, she was given a transfusion of 500 c.c. of blood, because of the anemia. Ferrous sulphate had already been started orally. By the eleventh day, her red blood count was 3,980,000 and the hemoglobin was 7.25 Gm. per cent. Clinically, she was much improved. The signs in her legs had disappeared, and on the fourteenth day, it was decided to decrease gradually the dosage of dicumarol, preliminary to discharging the patient.

A second transfusion of 500 c.c. of blood was given on the 19th hospital day. The prothrombin time was now near normal. On the 20th day, she suddenly became dyspneic and developed severe pleuritic pain in the left chest anteriorly and posteriorly. There was no evidence of recurrence of phlebothrombosis in the veins of the legs. A diagnosis of a second pulmonary embolus was made. The chest roentgenogram revealed the heart enlarged in the transverse diameter due to elevation of the diaphragms, and chronic passive congestion was evident in both lung fields, more marked at the right base. Dicumarol was again started, and it was planned to continue the drug until the onset of labor, and to resume anti-coagulant therapy after delivery. Because of the possible ill effects of dicumarol on the fetus, and the question of uterine hemorrhage at the time of delivery, it was decided to keep the prothrombin time on the low side (30 seconds) of the usually accepted therapeutic

*Thromboplastin was kindly furnished by Dr. Walter Hoskins of the Maltine Company.

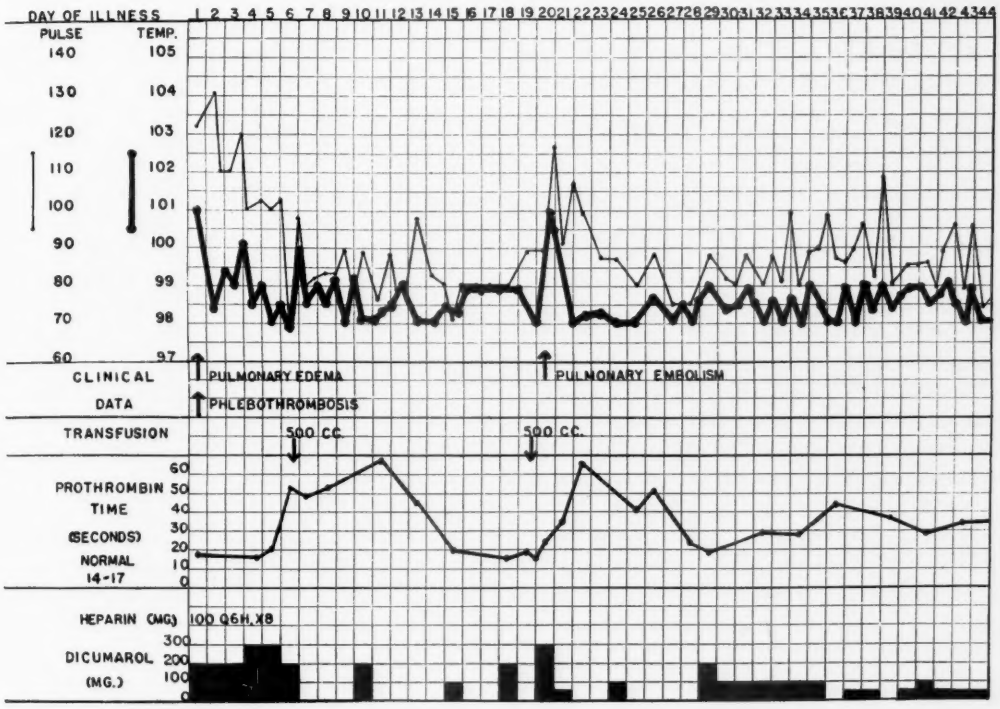


Fig. 1.—Clinical course.

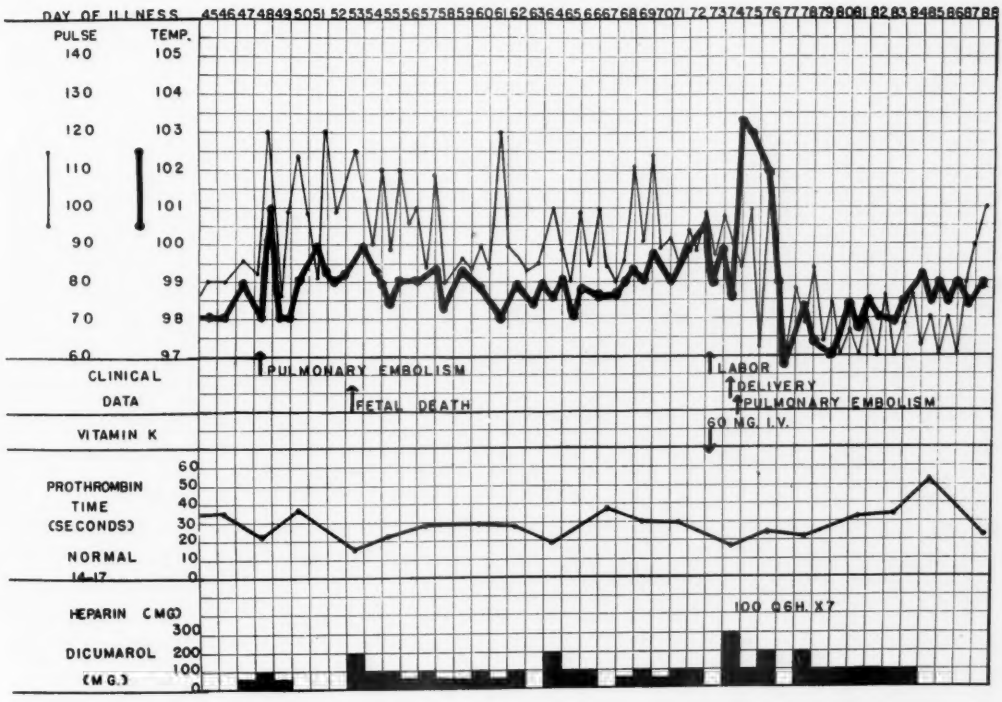


Fig. 2.—Clinical course (continued).

values. By the 23rd day, the thoracic pain had disappeared, and the patient was feeling well again. Repeated blood cultures were negative. There was no evidence of specific organic heart disease, but, in view of the episode of pulmonary edema, in association with the embolic episode on admission, digitalis was started. The patient was now ambulatory on the ward. On the 40th day, the red blood count was 3,540,000 and the hemoglobin was 10.3 Gm. per cent. On the 44th day, she noted pain above the mid-point of the left inguinal ligament. There was tenderness to deep palpation in this area, and a diagnosis of pelvic vein thrombosis was considered. At this time, the prothrombin time was 35 seconds. On the 48th day, she developed severe pain in the precordial region, which radiated to the left shoulder and arm, associated with dyspnea. A diagnosis was made of another pulmonary embolus. There was tenderness on pressure over the medial aspects of both thighs. On this day, the prothrombin time had been inadvertently allowed to fall to 21½ seconds. The following day, she appeared worse. The precordial pain was severe, and the dyspnea was marked. The patient was placed in an oxygen tent and given aminophylline, morphine, and papaverine, and by the next day, was much improved. She continued to be well until the 51st day, when she developed false labor pains which lasted for several hours. Two days later, on the 53rd day, the fetal heart became inaudible. There had been no previous indication of fetal distress. She was kept on dicumarol until the 73rd day, when labor began. Vitamin K, 60 mg., was given intravenously, and 21½ hours later she delivered a 6½ pound macerated stillborn baby boy. At delivery, the prothrombin time was 17½ seconds (normal = 14-17 sec.). There was no bleeding during the third stage of labor, and the usual oxytocics were given.

Several hours after delivery, the patient had a chill and the temperature rose to 103.8° F. She became dyspneic and cyanotic and again required an oxygen mask. Although examination of the chest was negative, another pulmonary embolus was suspected, and heparin and dicumarol therapy were resumed in doses as shown in Fig. 2. The patient improved rapidly, and the remainder of the postpartum course was uneventful. A roentgenogram of the chest made several days after this episode showed a wedge-shaped area of pulmonary consolidation extending from the left hilum to the first interspace, and prominence of the pulmonary artery.

The uterus involuted normally, and thrombosed pelvic or broad ligament veins could not be felt on bimanual examination. Dicumarol was continued for ten days after delivery and on the 14th postpartum day, the patient was discharged to the clinic. She has been followed for a period of four months after delivery and has been well. Examination of the heart has revealed essentially normal findings. The murmurs described on admission were still present, but of decreased intensity. The x-ray of the chest and electrocardiogram were normal. Her red blood count was 3,750,000, and hemoglobin was 13.3 Gm. per cent.

In summary, a 23-year-old multipara was admitted in the seventh month of pregnancy with a diagnosis of phlebothrombosis and pulmonary embolism. Because of three additional episodes of pulmonary embolism, each occurring as the prothrombin time was allowed to approach normal, it was necessary to continue dicumarol therapy through the last two months of pregnancy and the postpartum period. Intrauterine fetal death occurred on the 53rd hospital day, and on the 74th day, she delivered a stillborn macerated fetus.

Pathologic Examination of the Fetus

The body was that of a 2,640 Gm., 49 cm., badly macerated white male infant.

Head: There was considerable softening and overriding of the skull bones. Upon opening the skull, a large cephalohematoma was noted overlying both parietal bones. The brain was very mushy in consistency and a dull brown color throughout. There was no evidence of intracranial hemorrhage.

Chest: Upon the opening of the chest, extensive hemorrhage into the thymus gland was noted. The thymus was enlarged to about 4 by 4 by 4 cm. and was practically replaced by blood clot.

Heart: The pericardial sac contained about 15 c.c. of bloody fluid. The pericardium was normal. The myocardium was a dull light-brown color and the endocardium was normal.

Lungs: Both pleural cavities contained about 100 c.c. of dark bloody fluid. The lungs were retracted and rubbery in consistency. On section, there was no evidence of aeration. The surface was a uniform dark-red color.

Abdomen: The liver, spleen, pancreas, adrenals, and kidneys showed no evidence of hemorrhage, but were very soft in consistency. There was no hemorrhage in the gastro-intestinal or genito-urinary tracts.

Microscopic Examination.—

Lungs: The alveoli were nonexpanded, and numerous areas were seen where the alveolar mass contained epithelial debris and epidermoid type of cells. Areas of focal hemorrhage were present.

Thymus: The architecture of the thymus gland was completely disturbed by hemorrhage. The hemorrhage extended outward through the capsule and the entire gland was surrounded by diffuse hemorrhage. The normal architecture of the individual lobule was markedly disturbed by the extensive hemorrhage, so that the cells making up the gland were irregularly dispersed about the periphery of the lobule.

The remainder of the organs showed extensive autolytic changes.

Anatomical Diagnosis.—Massive hemorrhage of the thymus gland; focal hemorrhages of the lungs; bilateral hemothorax; hemopericardium; slight pulmonary aspiration of amniotic fluid; maceration with congestion and autolysis of all organs.

Discussion

On the basis of animal studies, already cited, it seems reasonable to assume that the fetal death was due to hemorrhage secondary to dicumarol. The findings at necropsy differed sufficiently from those usually found in the stillborn, following intrauterine asphyxia, to indicate an unusual cause for the fetal death. There appears to be little doubt that the extensive hemorrhage noted in the fetus was a direct effect of prolonged dicumarol therapy during the antenatal period. The mother had been maintained on dicumarol for fifty-three days prior to fetal death, and had received a total of 3,750 mg. of dicumarol.

Throughout the course, with few exceptions, the majority of the prothrombin time determinations were between 25 and 35 seconds. None of the determinations were abnormally high, and at no time did the patient show evidence of hemorrhagic phenomenon. Hence, it would seem that the fetus is more susceptible to the drug than the mother, and that maternal prothrombin determinations are not indicative of the fetal response to dicumarol. Quick[7] has previously pointed out this difference in susceptibility in the dog.

Two diagnostic features of thrombo-embolic disease were missing in this case. Hemoptysis was absent, and there was no roentgenographic evidence of pulmonary infarction until after delivery. Nevertheless, the patient on admission had typical signs and symptoms of phlebothrombosis, which had extended to the deep veins of the thigh. During the antenatal period, she was considered to have had episodes of pulmonary embolism, without infarction. However, the wedge-shaped shadow in the postpartum x-ray of the chest was characteristic of pulmonary infarction and confirmed the diagnosis of thrombo-embolism at least on this occasion.

An analysis of the clinical course (Figs. 1 and 2) reveals that the three pulmonary emboli which occurred while the patient was in the hospital developed on days when the prothrombin time had returned to normal. The

episode on the 20th day occurred at a time when dicumarol was purposely being reduced with a view to discontinuing it entirely. The episode on the 48th day occurred when the level was inadvertently allowed to return to normal, and the third embolus occurred a few hours after delivery, when the level again was normal, due to vitamin K administration. The embolus on the 20th day raises the question as to when anticoagulant therapy may be safely discontinued, and this is difficult to determine. From the clinical course, it would seem that anticoagulant therapy in this patient was necessary throughout the entire antepartum and postpartum period. The embolus of the 48th day and of the 74th day demonstrate again the importance in anticoagulant therapy of steering a safe course between hemorrhagic and coagulation levels. In this patient, embolization apparently occurred each time that the prothrombin level approached normal.

The absence of bleeding during delivery is noteworthy. The administration of 60 mg. of vitamin K intravenously at the onset of labor was able to return the prothrombin time to 17½ seconds at the time of delivery, 21½ hours later. Whether the absence of bleeding was due to the vitamin K, or to changes which occurred in the vessels of the placental-uterine junction, due to fetal death twenty-one days prior to delivery, is difficult to ascertain.

The question of venous ligation as the treatment of choice in this patient was considered. On her admission, the thrombotic process had already involved the deep veins of the thigh, and several examiners suspected pelvic vein thrombosis. This would have necessitated a high ligation, possibly of the vena cava, a procedure of considerable technical difficulty in the presence of pregnancy, if not entirely contraindicated, due to its possible untoward effect on the uterine circulation. Walsh and Barone[9] have reported two cases of antenatal phlebothrombosis, one with involvement of the left long saphenous and femoral veins, the other with involvement of the right long saphenous vein. Both patients were treated successfully with thrombectomy and ligation with uneventful recoveries. However, a search of the literature has failed to reveal any cases of antenatal phlebothrombosis that were treated with high venous ligation (high femoral, iliac, or vena caval), so that the effects of these procedures in the presence of pregnancy must be considered as unknown.

On the basis of our experience with this case, it is not possible to formulate a definite policy with regard to therapy for thrombo-embolic disease complicating pregnancy during the antenatal period. However, the danger to the fetus of prolonged therapy with dicumarol can be pointed out, since maternal prothrombin levels cannot be used as an index of the response of the fetus to this drug. Whether dicumarol can be used safely for a shorter period of time than in this case is not known. Whether prolonged therapy with heparin is equally dangerous to the fetus has not, to our knowledge, been determined.

Summary

1. A case of recurrent thrombo-embolic disease, occuring in a pregnant woman during the last two and one half months of her gestation, is reported.

2. The patient was treated continuously with dicumarol and on the 53rd day, after receiving 3,750 mg., the fetus died in utero.

3. Pathologic examination of the fetus revealed that death was due to hemorrhage, apparently caused by dicumarol.

4. Attention is drawn to the danger of fetal death from hemorrhage, which may result from the administration of dicumarol during the antenatal period.

References

1. Davis, A., and Porter, M.: Brit. M. J. **1**: 718, 1944.
2. Barnes, A. C., and Ervin, H. K.: Surg., Gynec. & Obst. **83**: 528, 1946.
3. Allen, E. V., Hines, E. A., Jr., Kvale, W. F., and Barker, N. W.: Ann. Int. Med. **27**: 371, 1947.
4. Schofield, F. W.: J. Am. Vet. M. A. **64**: 553, 1924.
5. Roderick, L. M.: J. Am. Vet. M. A. **74**: 314, 1929.
6. Roderick, L. M., and Schalk, A. F.: North Dakota Agr. Exp. Sta. Bull. **250**: 1, 1931.
7. Quick, A. J.: J. Biol. Chem. **164**: 371, 1946.
8. Shapiro, S.: Exper. Med. and Surg. **2**: 103, 1944.
9. Walsh, F. J., and Barone, A. M.: Illinois M. J. **91**: 305, 1947.

AN ANALYTICAL SURVEY OF MULTIGRAVIDAS

JAMES M. GEORGE, M.D., AND HOWARD A. POWER, M.D., PITTSBURGH, PA.

(From the Department of Obstetrics, University of Pittsburgh School of Medicine and the Elizabeth Steel Magee Hospital)

THIS paper deals with those patients who have had six or more pregnancies and is offered to refute the false feeling of security in the management of multigravidas. Dr. Bethel Solomons, in his paper, "The Dangerous Multipara,"[10] has stressed the numerous and occasionally serious implications of the various complications which are encountered in any large series of multiparous patients. The various assaults of successive pregnancies on the maternal organic systems and the residual pathology produced by preceding illnesses, all help to make the multigravida a poor risk. In this paper we have analyzed 783 pregnancies, parturitions, and puerperia of 500 multigravidas delivered at the Elizabeth Steel Magee Hospital, Pittsburgh, Pennsylvania, for the five-year period from Jan. 1, 1941, to Jan. 1, 1946.

At first glance, this subject would appear to be almost entirely a ward or free-clinic problem. That the treatment of the multigravida is not limited to this group is demonstrated by the fact that 27.2 per cent of women in their sixth and subsequent pregnancies were under the care of private physicians. In other words, every fourth patient is a potential problem for the obstetrician in private practice and should be watched even more carefully than the primigravida on whom his attention is usually focused. As Dr. Solomons stated in his paper, "Pregnancy is definitely a case where practice does not make perfect."[10]

Gravidity

Of the 783 deliveries studied, 237 (30.2 per cent were sextigravidas, 205 (26.2 per cent) septigravidas, 129 (16.5 per cent) octigravidas, 87 (11.2 per cent) nonigravidas, and 61 (7.7 per cent) decigravidas. The remaining 64 women had had from 11 to 25 pregnancies. This latter classification formed 8.2 per cent of the total deliveries.

GRAVIDITY

GRAVIDA	NUMBER	PER CENT
vi Sextigravidas	237	30.2
vii Septigravidas	205	26.2
viii Octigravidas	129	16.5
ix Nonigravidas	87	11.2
x Decigravidas	61	7.7
xi to xxv	64	8.2
Total	783	100.0

Types of Delivery

A total of 620 normal children resulted from the 783 deliveries with 62 additional stillbirths and neonatal deaths, and 101 abortions. There were 573

spontaneous births, 23 low forceps, 6 midforceps, 38 breech extractions, 25 versions and extractions, 16 cesarean sections, and 1 craniotomy with extraction.

TYPES OF DELIVERY

MULTIGRAVIDAS	NUMBER	PER CENT	GENERAL HOSPITAL* NUMBER	GENERAL HOSPITAL* PER CENT
Spontaneous	573	84.0	1370	41.9
Low forceps	23	3.4	1360	41.6
Midforceps	6	0.9	99	3.0
Breech extractions	38	5.6	107	3.2
Internal podalic version and extraction	25	3.7	165	5.0
Cesarean sections	16	2.3	171	5.2
Craniotomy and extraction	1	0.1	2	0.06

*Hospital averages are figured from 3,274 deliveries in the Elizabeth Steel Magee Hospital from Jan. 1, 1945, to Jan. 1, 1946.

It is to be noted that there was a considerably higher percentage of spontaneous deliveries and a greatly lower percentage of low forceps deliveries in the multigravidas. This is explained by the fact that the ward multigravidas are largely delivered by students and the general hospital figures include primigravidas, both private and ward, who are usually delivered by prophylactic outlet forceps. A higher percentage of breech deliveries in the multiparas indicates a greater frequency in these patients. The hospital general average cesarean section rate is over twice that of the multigravida section rate.

Morbidity and Mortality

The maternal morbidity is much higher in the grandipara than in the primipara and in the gravida v and under, as is indicated by the increased hospital days. The average period of hospitalization for private patients (primiparas and multiparas) over the last five-year period has been twelve days, while that for ward patients has been eight days. The average hospital stay for all patients has been 10 days. It might be stated here that hospitalization of ten to twelve days in private patients does not always indicate morbidity but merely a desire for additional rest, while. in the free clinic patient, hospitalization over the average usually indicates morbidity. The average hospital stay for multiparas, including private and ward cases, is 12.4 days. In other words, the morbidity of the multipara necessitates an increased hospitalization of 2.4 days per patient.

There is no accurate way of estimating fetal morbidity and the harm done to babies at delivery. Rank[9] has advanced the theory that many cases of mental disease date from trauma to the fetal skull at birth.

The maternal mortality is atrociously high in that there were seven deaths in 500 mothers, or a mortality rate of 1.4 per cent. This percentage is seven times that of our average maternal mortality rate of 0.261 per cent at the Elizabeth Steel Magee Hospital (67 deaths in 25,623 deliveries from Jan. 1, 1941, to Dec. 31, 1946). This latter mortality rate compares favorably with that in other maternity centers.

MORTALITY RATES

Magee Hospital, 1941 to 1947	2.6 per 1000 births
Multigravidas, gravida vi and over	14.0 per 1000 births
Pittsburgh, Pa.[11]	1.5 per 1000 births
Chicago Lying-in Hospital[7]	1.7 per 1000 births
Philadelphia, Pa., 1931 to 1933[12]	4.4 per 1000 births
National total, 1941[12]	2.7 per 1000 births

The causes of death are listed below. It will be noted that two deaths followed tubal ligation on the seventh and ninth postpartum days. Sterilization

is now done within six to eight hours after delivery or is postponed until complete involution of the pelvic organs has occurred.

DEATHS IN MULTIPARAS

	GRAVIDA	CAUSE OF DEATH
1.	vi	Septic abortion, pelvic thrombophlebitis, pulmonary infarcts
2.	vi	Essential hypertension, cerebral accident (before delivery)
3.	vii	Tubal ligation seventh postpartum day, pulmonary emboli
4.	viii	Sulcus tear with septicemia and fulminating peritonitis, pulmonary emboli
5.	viii	Tubal fulguration ninth postpartum day, pulmonary emboli
6.	ix	Uterine atony, uncontrollable postpartum hemorrhage
7.	x	Nephritic hypertension, uremia

As we study the fetal mortality in this series, it is found that there were 62 deaths in 682 births, or 9.1 per cent. If the 12 macerated fetuses and 13 nonviable infants are deducted, the corrected fetal mortality becomes 5.4 per cent. The causes of death as indicated on the hospital charts are listed below.

FETAL MORTALITY

MULTIGRAVIDAS				HOSPITAL AVERAGE
Stillbirths		29	4.2 per cent	2.3 per cent
Macerated stillbirths		12	1.7 per cent	1.3 per cent
Prematures (nonviable)	13		1.9 per cent	0.7 per cent
Died		21		
Atelectasis	2			
Congenital anomaly	1			
Respiratory failure	1			
Emphysema	1			
Anoxia	1			
Jaundice	1			
Septicemia—				
Cellulitis of scalp	1			
Uncorrected fetal mortality:		62 deaths in 682 births, or 9.1 per cent		7.4 per cent
Less prematures and macerated stillbirths:		25		
Corrected fetal mortality:		37 deaths in 682 births, or 5.4 per cent		5.3 per cent

It is readily noted that the percentages of stillbirths, macerated stillbirths, and nonviable prematures in the multigravidas are higher than in the hospital general average.

There were, in addition, 98 spontaneous and induced, and 3 therapeutic abortions in the 783 pregnancies studied. Without a doubt, there were other spontaneous complete abortions in this group of 500 patients which did not necessitate hospitalization.

There was then, in this series, 1 abortion to every 7.8 births, or 12.8 per cent. This figure approximates Bland and Montgomery's[1] estimate that one pregnancy in five ends in abortion.

ABORTIONS

	MULTIGRAVIDAS		HOSPITAL AVERAGE	
Spontaneous and induced	98	12.8 per cent	271	8.27 per cent
Therapeutic	3	0.38 per cent	13	0.39 per cent

Toxemias

According to the literature, the expected incidence of pre-eclampsia is from 10 to 15 per cent, and the disease is seen more frequently in primiparas. When

pre-eclampsia does occur in multiparas, pre-eclampsia and the occasional resultant eclampsia have been said to be more severe and to offer a poorer prognosis than in the primipara. There were 49 pre-eclamptics in this series of patients, seven of whom went into true eclampsia (one or more convulsions). Two of the seven had postpartum eclampsia. There were no maternal deaths from this complication. The fetal toll was approximately 40 per cent. There were 27 cases of nephritic toxemia and 41 cases classified as essential hypertension. Possibly the latter two types of disease may be attributed partially to the increased ages of the gravidas. Mild nausea and vomiting necessitating hospitalization was not encountered. There were seven cases of pernicious nausea and vomiting (hyperemesis gravidarum), which did require hospitalization. All of these patients were treated successfully by conservative therapy. The table below gives a comparison of the incidence of the toxemias of pregnancy in multigravidas and in the Elizabeth Steel Magee Hospital. The percentage columns indicate that all of the toxemias occur in greater frequency in the multigravida than in the average hospital patient at the Elizabeth Steel Magee Hospital.

INCIDENCE OF VARIOUS TYPES OF TOXEMIAS OF PREGNANCY

TOXEMIAS	MULTIGRAVIDAS		MAGEE HOSPITAL	
Pre-eclampsia	42	5.4 per cent	79	0.24 per cent
Eclampsia	7	0.8 per cent	5	0.15 per cent
Nephritic toxemia	27	3.4 per cent	31	0.94 per cent
Essential hypertension	41	5.2 per cent	23	0.70 per cent
Hyperemesis	7	0.8 per cent	21	0.64 per cent

Placenta Previa and Premature Separation

The dangers to both mother and offspring associated with placenta previa and premature separation are well known. The frequency of placenta previa and premature separation given by various sources varies greatly. Bland and Montgomery[2, 3] stated that one case of placenta previa is seen in every 100 pregnancies (1 per cent) and that premature separation occurs once in every 300 pregnancies (0.3 per cent). At the Elizabeth Steel Magee Hospital, in 16,737 deliveries there were 156 cases of placenta previa, or one in 107 pregnancies (0.9 per cent). There were in the same number of deliveries 211 cases of premature separation of the normally implanted placenta, or one in 79 (1.2 per cent).

In the multiparas studied, 12 cases of placenta previa, or one in 57 deliveries (1.7 per cent), and 14 cases of premature separation, or one in 48 normal births (2.0 per cent), were encountered. These figures should indicate conclusively that both of these complications are more frequent in the multiparas and especially in gravidas vi and over.

INCIDENCE OF PLACENTA PREVIA AND PREMATURE SEPARATION

	BLAND AND MONTGOMERY[2, 3]	MAGEE HOSPITAL		MULTIGRAVIDAS	
Placenta previa	1.0 per cent	156	0.9 per cent	12	1.7 per cent
Premature separation	0.3 per cent	211	1.2 per cent	14	2.0 per cent

With these complications, the fetal mortality is likewise appallingly high. In many instances the fetuses die in utero as a result of anoxia.

Abortion

Abortion has been discussed under morbidity and mortality.

Hydatid Mole and Ectopic Pregnancy

One hydatid mole and one ectopic pregnancy were encountered in this series. Each was handled uneventfully following accepted techniques.

Retained Placental Tissue

There were 13 cases of retained placenta. The placentas were removed manually either immediately following delivery or after an interval of one hour. Thirty cases of severe secondary anemia were encountered which necessitated giving 25 transfusions. Only one transfusion reaction resulted. Retained placenta occurred only slightly more frequently in multigravidas than in the hospital average, while over six times as many transfusions post partum were deemed necessary for the multigravidas as for the average hospital patient.

INCIDENCE OF RETAINED PLACENTA

	MAGEE HOSPITAL		MULTIGRAVIDAS	
	CASES	PER CENT	CASES	PER CENT
Retained placenta	34	1.0 per cent	13	1.5 per cent
Severe anemia	18	.55 per cent	30	3.8 per cent

Disproportion

There is a tendency for each successive baby to be larger than its predecessor. Usually the maternal pelvis will accommodate a slightly larger passenger, but disproportion can arise insidiously with frequent fetal injury or death.

Malpresentation

In considering malpresentations and complications of presentations, there were nine sets of twins, or one in 75 pregnancies, or an increase over the expected frequency of one in 85 to one in 100 pregnancies, as given by Bland and Montgomery[4] and DeLee and Greenhill,[8] respectively. Thirty breech presentations (3.8 per cent) were encountered, which is slightly more than the average incidence of 3 per cent. We find a greatly increased proportion of transverse lies with shoulder presenting. There were eight such presentations or one in 85 deliveries, which is more than twice the expected frequency of one in 200 pregnancies. Two face presentations, or 1 in 341, were encountered, which is somewhat less than the expected frequency of 1 in 200 to 1 in 300 cases. That we get anomalous presentations in the grandipara is to be expected because of an atonic uterus and the relaxed abdominal musculature so frequently found. These malpresentations, if not recognized and treated early, definitely lead to both increased fetal and maternal mortality.

Birth Weights

The average weight of a term newborn baby is generally accepted as being 7 to 7½ pounds. The average weight of the babies in this series is 7 pounds, 6 ounces, excluding prematures and twins. The largest baby in this series weighed 11 pounds, 2 ounces, and was the eleventh child of a 35-year-old mother. The smallest term baby delivered of these multigravidas weighed 5 pounds and was the ninth child of a patient with nephritic toxemia.

Length of Labor

The length of labor in multigravidas is of considerable interest and practical importance to the obstetrician. In addition, the length of labor is one indicator of the type of uterine contractions which have preceded delivery. The average length of labor in the multipara is usually considered to be about 12 hours. In our series, the shortest labor recorded was 16 minutes, while the longest labor was 96 hours and 25 minutes. The over-all average length of labor was 12 hours and 48 minutes. Arbitrarily, we have considered for purposes of comparison

a labor of one hour or less to be precipitate and that of twenty hours or longer to be inertial in type. There were three times as many precipitate labors in the multigravidas as were encountered in the general hospital average. On the other hand, the number of inertial labors encountered was about the same in both groups.

ANOMALOUS PRESENTATIONS, BIRTH WEIGHT OF BABY, AND LENGTH OF LABOR

	AVERAGE	MAGEE HOSPITAL	MULTIGRAVIDAS
Presentations:			
Breech	3.0 per cent	107 3.2 per cent	30 3.8 per cent
Transverse[5]	0.5 per cent	9 0.27 per cent	8 1.0 per cent
Face[6]	0.5 per cent	9 0.27 per cent	2 0.2 per cent
Birth Weight:	7 to 7½ pounds	Unobtainable	7 pounds, 6 ounces
Labor:	10 to 12 hours	*Inertial* 504 15.3 per cent *Precipitate* 15 0.45 per cent	*Shortest,* 16 min. *Longest,* 96 hours, 25 minutes *Inertial* 102 14.9 per cent *Precipitate* 9 1.3 per cent

Because of the difficulty of determining when the grandipara is actually in labor, many are admitted in false labor with resulting useless cost to the patient and hospital. Thirty such patients in false labor were admitted for a day or so and then discharged.

Syphilis and Tuberculosis

Syphilis was found in 27 gravidas. Some of these cases were diagnosed by routine serologic examinations, while others were known syphilitics and had received more or less antisyphilitic therapy. Four patients with tuberculosis were followed very closely in our antepartum clinics and were delivered uneventfully.*

The incidence of tuberculosis and syphilis varies with the geographical location and the financial status of the group studied. Contrary to what might be expected, our ward (multigravida) incidence of tuberculosis is lower than the hospital average. This is probably explained by the fact that few tuberculous patients are physically able to have as many as six children.

SYPHILIS AND TUBERCULOSIS

	GENERAL AVERAGE	MAGEE HOSPITAL		MULTIGRAVIDAS	
	VARIES WITH LOCATION	NUMBER	PER CENT	NUMBER	PER CENT
Syphilis	3—10 per cent	89	2.7	27	3.4
Tuberculosis	1 per cent	22	0.67	4	0.51

Incidental Complications

There were 23 cases of bronchitis and upper respiratory infections which necessitated special therapy and which were noted on the hospital charts as complications. In addition, four cases of pneumonia, one case of pneumonitis, and one case of bronchiectasis complicated pregnancy and labor. Three cases of appendicitis and one case of cholecystitis necessitated appendectomy and cholecystectomy respectively. Other infections complicating pregnancy and

*The Tuberculosis League Hospital of Pittsburgh acts as our consultant in all cases of tuberculosis.

labor and of sufficient severity to be recorded are listed below. All of these infections were treated either by a separate specialty clinic or by the obstetric clinic.

INFECTIONS COMPLICATING PREGNANCY AND LABOR

Amnionitis	1
Appendicitis, acute, with appendectomy	3
Bronchiectasis	1
Bronchitis	23
Cholecystitis with cholecystectomy	1
Cystitis	2
Lymphogranuloma inguinale	1
Nephritis and pyelonephritis	10
Nephrolithiasis	1
Poliomyelitis with paralysis (right leg)	1
Pneumonia	4
Psoriasis	1
Pyelitis	3
Salpingitis, chronic	1
Syphilis	27
Syphilis, meningovascular	1
Thrombophlebitis, pelvic	1
Tuberculosis	4

The infections complicating the puerperium are similarly listed below and need little explanation, except to say that they occurred in this series.

INFECTIONS COMPLICATING THE PUERPERIUM

Abscess, axillary	1
Abscess, right femoral triangle	1
Appendicitis, with appendectomy	3
Cellulitis, pelvic	1
Cystitis	2
Endometritis	18
Infarcts, lungs, septic	1
Influenza	1
Mastitis with abscess formation	14
Necrobiosis (fibroid)	1
Phlebitis	1
Pneumonia	1
Tapeworm	1

Other Complications

Besides the toxemias, hemorrhages, and infections which have already been discussed, there were certain other medical complications which were encountered. Four asthmatics had to be hospitalized during their pregnancies. The grandipara is very prone to develop painful varicosities. There were 16 cases recorded, although there must have been many more. There were 12 patients with cardiac disease, 8 cases of which were rheumatic in type. Two were in congestive failure. In this rather small group of cases there were two cases of cerebral embolus with resulting hemiplegia. Only one diabetic was encountered. Two colloid goiters were diagnosed among these patients. Two patients were diagnosed as having generalized malnutrition and emaciation. One case each of Banti's disease and idiopathic enlargement of the liver were found. One patient had an inoperable medulloblastoma of the brain. Certainly no one would say that these medical problems were improved by the added strain of pregnancy.

Multigravidity is not, per se, an indication for sterilization. In this series there were 47 postpartum ligations, seven tubal fulgurations, one tubal resection, and one hysterectomy by maternal and paternal consent.

Summary

1. A total of 783 pregnancies of 500 consecutive multigravidas, gravida vi and over, are analyzed.

2. One-fourth of these are private patients.

3. Maternal morbidity is increased, necessitating an average increased hospitalization of 2.4 days per patient.

4. The maternal mortality rate is seven times that of the average mortality rate.

5. Fetal mortality is high in the multigravida, and the morbidity cannot be estimated.

6. Toxemias in the grandipara are increased over the average expectancy.

7. The frequency of placenta previa and premature separation is greater in the multigravida.

8. Malpresentations increase maternal and fetal mortality.

9. False labors are common in the multigravida.

10. Infections are prominent as causes of morbidity in the multigravida in pregnancy, labor, and the puerperium.

11. Medical complications other than those summarized above, which require treatment, are found frequently.

References

1. Bland, P. Brooke, and Montgomery, Thaddeus L.: Practical Obstetrics, ed. 3, Philadelphia, 1940, F. A. Davis Co., page 264.
2. Bland, P. Brooke, and Montgomery, Thaddeus L.: Practical Obstetrics, ed. 3, Philadelphia, 1940, F. A. Davis Co., page 251.
3. Bland, P. Brooke, and Montgomery, Thaddeus L.: Practical Obstetrics, ed. 3, Philadelphia, 1940, F. A. Davis Co., p. 241.
4. Bland, P. Brooke, and Montgomery, Thaddeus L.: Practical Obstetrics, ed. 3, Philadelphia, 1940, F. A. Davis Co., p. 142.
5. Bland, P. Brooke, and Montgomery, Thaddeus L.: Practical Obstetrics, ed. 3, Philadelphia, 1940, F. A. Davis Co., p. 363.
6. Bland, P. Brooke, and Montgomery, Thaddeus L.: Practical Obstetrics, ed. 3, Philadelphia, 1940, F. A. Davis Co., p. 364.
7. Davis, M. E., and Gready, T. G., Jr.: Am. J. Obst. & Gynec. 51: 492-513, 1946.
8. DeLee, Joseph B., and Greenhill, J. P.: Principles and Practice of Obstetrics, ed. 9, Philadelphia, 1947, W. B. Saunders Co., page 417.
9. Rank, O.: Birth Trauma Theory, London, 1929, Harcourt, Brace and Co.
10. Solomons, Bethel: Med. Klin. 25: 1784, 1930.
11. Bureau of Infectious Diseases, Department of Public Health, Pittsburgh, Pa. Annual Report, Vital Statistics, 1946.
12. Maternal Mortality in Philadelphia, 1931-1933. Report of Committee on Maternal Welfare. Philadelphia County Medical Society, 1934.

A CULTURAL METHOD FOR THE DIAGNOSIS OF TRICHOMONAD INFESTATIONS

J. Jerry Lash, A.B., and Elmer Belt, M.D., Los Angeles, Calif.

THE criterion of diagnosis in the symptom syndrome known clinically as "trichomonad vaginitis" has been the proper identification of the vaginal flagellate, *Trichomonas vaginalis*. There is general agreement among authors that the various clinical manifestations are easily recognized and are common.[11] The most frequent subjective complaint is the presence of a vaginal discharge, with an increase of vaginal discomfort prior to and following the menstrual period.[9] The annoying and copious leucorrhea is at times watery, foaming, or frothing, and almost always malodorous. Some patients complain of mild burning on urination associated with mild frequency. These signs coupled with the demonstration of motile trichomonads in a hanging-drop preparation made from the vaginal discharge are sufficient evidence of trichomonad vaginitis for the institution of trichomonicidal therapy; however, in some instances, the persistent and refractory leucorrhea has failed to reveal the offending organisms in a wet-mount.

During the past eighteen months, an extensive research program designed to correlate varied bacterial constituents found in diverse pathological conditions of the genitourinary tract has been in progress.[6] One major study has been directed toward symbiotic relationships between vaginal bacterial elements and the flagellate, *Trichomonas vaginalis*, and during investigations in this direction, a new medium for the isolation and propagation of *Trichomonas vaginalis* has been developed and reported.[7] Since methods used in diagnosing 58 clinical cases for research studies have been sufficiently successful, it seemed desirable to make our procedures available to other workers in the field. This report deals with a clinical and laboratory approach to the problem, using a cultural method as a routine aid for the diagnosis of trichomonad infestations.

Material and Methods

The area surrounding the genitals is cleansed carefully by washing with green soap solution followed by distilled water. A sterile vaginal speculum, preferably unlubricated, is introduced, exposing the lower genital tract. The condition of the labia, vaginal mucosa, and cervix is noted as well as the character, color, odor, and amount of discharge present. Specimens for examination are drawn on cotton-tipped applicator swabs which are passed beyond the speculum blades, care being exercised not to touch the blades upon withdrawal of the swabs. The material is distributed directly to slides for wet-mounts, Gram's and iron-hematoxylin stained preparations, also to culture tubes containing 8 to 10 ml. of flagellate isolation medium (F.I.M.).[7]

The wet-mount is prepared by emulsifying a drop of the vaginal discharge in a drop of normal saline placed in the center of a glass slide which previously has been heated so that it is comfortably warm when touched to the back of the hand. The emulsion is mixed thoroughly with a wooden applicator stick or bacterial wire loop. A coverslip is placed at an angle to the slide with one edge

near the drop but not quite touching it. The coverslip is then pushed along the surface of the slide until the edge contacts the drop allowing a small portion of the material to spread along the edge. The coverslip is finally allowed to drop upon the slide, drawing the fluid portion of the drop beneath the coverslip by capillary attraction thus excluding gross particles in the specimen. This method has provided satisfactorily thin and even preparations in all cases. Microscopic examination is made using the low and high dry objectives, with the substage diaphragm almost closed.

One drop of a 0.10 per cent solution of safranine in normal saline placed along the edge of the coverslip on the mount is drawn into the fluid portion under examination and provides a contrasting field for observation. We have found this concentration of dye nontoxic to the flagellates in wet-mounts over the period of time usually required for microscopic examination.

A smear is prepared for Gram's stain by emulsifying another drop of material in a drop of normal saline, and spreading the mixture evenly over two-thirds of the surface of a clean slide using a bacterial wire loop. Drying and fixing of the smear are accomplished in the usual manner. The Hucker modification[5] of the Gram's stain has given us consistently good results and makes possible the recording, for research data, of the type of bacterial flora present, according to the modified classification of Loeser,[8] as follows:

Type I: Gram-positive vaginal bacilli only.

Type II: Gram-positive vaginal bacilli plus mixed organisms including coccobacilli, diplococci, variable commas, streptococci, etc., and,

Type III: *No* Gram-positive vaginal bacilli, with disappearance of the variable commas and a predominance of cocci of all varieties.

The Gram-stained smear also serves to exclude gonococcal infections. It is routinely followed by culture on chocolate agar. Growths are confirmed by the oxydase test and fermentation subcultures.

Stained mounts are made and reserved for investigation if flagellates are not found in the wet-mount, and for examination while cultures are undergoing incubation. Faust's[4] iron-hematoxylin staining method is used, preceded by wet-fixation in Schaudinn's sublimate solution.

Until recently, culturing of vaginal discharges for trichomonads has been inconvenient since a practical medium adequately supporting their growth and permitting reproduction in a short period of time has not been available. Numerous simple media designed for the propagation of routine laboratory stock strains (e.g., Cleveland-Collier liver infusion medium,[3] Boeck and Drbohlav Locke egg serum medium[2]) have not been found sufficiently nutritive for rapid cultivation, and consequently have been inadequate as a laboratory diagnostic aid. A more desirable medium must contain necessary growth factors, be easily prepared, and must be capable of supporting growth and reproduction of flagellates from a minute inoculum containing very few flagellates.

Such a medium has been devised for the primary isolation of trichomonads from vaginal discharges and has been used in our laboratories for over one year. Although some authors have reported that trichomonads have never been found in cultures made from material diagnosed as "negative" by wet-mount (Stein and Cope,[10] Bland et al.[1]), we have diagnosed seven such "negative" wet-mounts as confirmed "*positive*" clinical cases after suitable culture of the material.

The medium, described in a previous communication,[7] consists of a 2:3 serum-Ringer's solution with an equal part of a 1 per cent solution of an enzymatic yeast protein hydrolysate ("Prominogen") containing added agar, carbohydrates, and liver extract. The following procedure is used:

A sterile swab carrying a small quantity of the discharge material is placed in 10 ml. of F.I.M.-hydrolysate medium[7] contained in a plugged 20 by 150 mm.

culture tube. An alternative procedure involves the preparation of tubes containing the medium with a specimen swab wound directly into the cotton plugging the test tube. When collecting the specimens, this swab is moistened with the medium and passed through the speculum. After the discharge material has been collected on it, the swab is replaced directly in the tube of medium. Using either procedure, the culture is incubated after thoroughly mixing the specimen with the fluid medium. Incubation is maintained at 37 to 37.5° C. for 24 hours, after which time a drop of the sediment at the bottom of the medium is removed with a wide-mouthed bulb-type pipette. This is made up as a wet-mount, and is examined for trichomonads as was done with the original material. If trichomonads are not observed, the tube is returned to the incubator for an additional 24 hours. Following the second incubation period, the tube is gently shaken and rotated to mix all of the sediment with the fluid medium, and the entire contents are transferred to a 15 ml. centrifuge tube. After centrifugation at 1,200 r.p.m. for 15 minutes, the supernatant liquid is poured off, and the entire sediment mounted on a slide for examination as before.

The following two cases exemplify the use of the cultural method.

Report of Cases

CASE F-48.—Aged 41 years, married. The patient entered the office complaining of a recurrent trichomonad vaginitis which had been diagnosed by Dr. A., who believed that the urinary tract was the source of reinfection. A general physical examination revealed little of interest. Examination of the genitals showed a deep vagina exuding a profuse mucopurulent discharge. The cervix was large, firm, movable, and contained no masses. Urethral strippings showed no trichomonads in a wet-mount; however, smears from the vaginal discharge revealed an occasional trichomonad. Catheterized bladder urine had a specific gravity of 1.011, pH 5.6, and contained no albumin or sugar. Microscopic examination revealed an occasional white blood cell per high-power field, no red blood cells or casts, and a few epithelial plates in the sediment. No trichomonads were noted, and a Gram-stained mount revealed no bacteria.

A careful study of the bladder at this time revealed a diffuse injection of the entire area. The ureteral orifices readily admitted No. 4 ureteral catheters. Specimens of urine collected through these ureteral catheters revealed no trichomonads or bacteria. The patient was instructed to return for a morning urine examination. The total specimen of 430 ml. urine was distributed to tubes and centrifuged at 1,200 r.p.m. for 15 minutes. Carefully studied wet-mounts of the sediment revealed no trichomonads. The pooled sediments were distributed to four tubes of F.I.M.-hydrolysate medium which were incubated at 37.5° C. Duplicate plates of Sabouraud's dextrose agar were streaked; one incubated at room temperature, the other at 37.5° C. After one week of incubation, neither Sabouraud plate revealed evidence of mycological elements. The cultured morning urine specimen showed myriads of trichomonads after forty-eight hours.

To eliminate another possible source of infection, the patient's husband was examined. Physical findings were essentially negative. A urine specimen (No. 2 in "three glass test") had a specific gravity of 1.018, pH 5.2, and no albumin or sugar. Microscopic examination of the centrifugalized sediment revealed a rare white blood cell per high-power field, an occasional epithelial cell and no trichomonads. A Gram-stain showed no bacteria.

CASE LR-8.—Aged 34 years, married. Mrs. R. complained of constant pain in the urethra not associated with burning or frequency, and soreness in both costovertebral angles. A general physical examination was negative. Pelvic examination revealed a normal clitoris, urethra, and vagina. The cervix was badly lacerated. Catheterized bladder urine had a specific gravity of 1.010, pH 4.8, no albumin or sugar, and microscopically showed 5 to 7 white blood cells per high-power field, one red blood cell per high-power field, mucus and

an occasional squamous epithelial cell. A Gram-stained mount of the sediment revealed some Gram-positive cocci. A wet-mount and iron-hematoxylin stained smear of the vaginal discharge were negative for trichomonads.

An upper urinary tract study revealed normal renal pelves and ureters on both sides. Cultures of ureterally catheterized urine revealed Gram-positive cocci in abundance but no trichomonads were observed.

Twelve days later, the patient returned complaining of a vaginal discharge. Hanging-drop preparations made at this time were carefully examined by two independent observers and revealed no trichomonads, but swabbings of the vaginal and cervical secretions cultured in F.I.M.-Hydrolysate medium as described revealed many flagellates following incubation at 37.5° C. for forty-eight hours.

Material obtained from the cervix was plated to Sabouraud's dextrose agar and examination after one week at room temperature revealed numerous pasty, spready, white, sour-smelling colonies closely resembling *Monilia*. Subcultures and confirmation tests (fermentations, differential media, etc.) readily identified the organism as *Monilia albicans*.

Of interest is the fact that with successful treatment of the monilial infection, the vaginal trichomonad infestation also disappeared, but recurred intermittently for a period of five months. On three occasions, although no trichomonads were noted in the wet-mount, they were recoverable upon culture of the material.

Summary

By usual laboratory methods, 51 cases of trichomonad vaginitis in 58 studies were diagnosed. The use of a yeast protein hydrolysate-enriched medium permitted the remaining so-called "negative" cases to be culturally diagnosed as "positive" *Trichomonas vaginalis* infestations. A systematic laboratory protocol has been outlined, and the use of a cultural method is discussed and advocated as an aid in diagnosis. Two typical case reports are presented.

References

1. Bland, P. B., Goldstein, L., and Wenrich, D. H.: J. A. M. A. **96**: 157-163, 1931.
2. Boeck, W. C., and Drbohlav, J.: Am. J. Hyg. **5**: 371-407, 1925.
3. Cleveland, L. R., and Collier, J.: Am. J. Hyg. **12**: 606-613, 1930.
4. Faust, E. C.: Cited in Craig, C. F.: Laboratory Diagnosis of Protozoan Diseases, Philadelphia, 1942, Lea & Febiger, p. 49.
5. Kolmer, J. A., and Boerner, F.: Approved Laboratory Technic, ed. 4, New York, 1945, D. Appleton-Century Co., p. 376.
6. Lash, J. J.: Manuscript in preparation.
7. Lash, J. J.: Am. J. Trop. Med. **28**: 111-119, 1948.
8. Loeser, A.: Zentralbl. f. Gynäk. **44**: 417-429, 1920.
9. Salberg, J. B., and Brunet, W. M.: Virginia M. Monthly **63**: 223-227, 1936.
10. Stein, I. F., and Cope, E. J.: Am. J. Obst. & Gynec. **24**: 348-354, 1932.
11. Winther, N.: J. Iowa M. Soc. **27**: 407-410, 1937.

1893 Wilshire Blvd.

OVARIAN TUMORS AND UTERINE BLEEDING*

M. A. Bayly, M.D., and R. R. Greene, M.D., Chicago, Ill.

(From the Department of Obstetrics and Gynecology, Northwestern University Medical School and Wesley Memorial Hospital)

IT HAS been assumed that some hormone-producing tumors of the ovary cause abnormal uterine bleeding, and it is widely accepted that nonhormone producing tumors may occasionally have the same effect. Since there have been few adequate attempts to explain the exact relation of these latter tumors to abnormal uterine bleeding, our original objective was to determine the nature of this relationship. As will be demonstrated, this objective was not attained. In fact, it was found that abnormal bleeding was not common, and when present was, in most instances, due to demonstrable intrauterine pathology, and not to the ovarian tumor.

Literature

Koucky,[9] Mayer,[12] Lippert,[10] Fauvet,[6] Moulonguet-Doléris,[14] Marwil,[11] and many others have reported instances of menstrual irregularity as "due" to ovarian tumors (dermoids, Brenner tumors, serous and pseudomucinous cystadenomas, and ovarian carcinomas). Meyer[13] suggested that abnormal bleeding might result from a metabolic upset in the ovary caused by the tumor growth. Moulonguet-Doléris postulated that the tumors disturbed the nerve supply of the ovary, thus interfering with its function and secondarily effecting endometrial changes.

According to Berkeley, White, and Cook,[2] ovarian tumors may cause postmenopausal bleeding and menstrual abnormalities. Bourne and Williams[3] agree, particularly insofar as postmenopausal bleeding is concerned.

Geist[7] reported abnormal bleeding in over 40 per cent of 1,096 ovarian neoplasms of all types. His explanation was that "complicating local physical factors associated with uterine displacement and congestion are usually responsible."

Te Linde[19] studied the general subject of postmenopausal bleeding; his series included 349 patients. He apparently believed that the bleeding was caused by benign nonhormonal tumors in eight. An additional eight malignant neoplasms were associated with bleeding but there was carcinoma in the uterus of five of them.

In a similar study of 406 postmenopausal bleeders, Taylor and Millen[18] noted 23 instances of bleeding associated with ovarian neoplasms. However, intrauterine pathology was found in all but nine. Four of the latter were granulosa-cell tumors, and of the remaining five nonhormonal tumors, the uterus was not available in at least one.

In a study of the postmenopausal endometrium, Novak and Richardson[15] concluded that with the exception of known hormone-producing ovarian tumors, ovarian neoplasms do not affect the endometrium; their occasional association with endometrial hyperplasia is probably a coincidence.

Several authors have granted that these tumors may be associated with abnormal bleeding, but have suggested that the bleeding was due to an unrecognized granulosa-cell tumor, or possibly a misinterpreted functioning neoplasm.

*Supported in part by a grant from Ciba Pharmaceutical Products Inc.

The latter suggestion is R. Meyer's[13]; the former, G. van S. Smith's.[17] Unless we misinterpret them, both Payne,[16] and Bourne and Williams[3] infer that these tumors may have unrecognized ability to produce hormones. With this in mind, Adair and Watts[1] investigated the hormone content of ovarian cyst fluids and found "no results which warrant conclusions."

Material

Tissues were available from 154 patients with cystic or solid nonhormone-producing ovarian tumors. For the purpose of this study it was necessary also to have access to the uterine tissues. Since many of these tumors were benign and from relatively young women, hysterectomy had not always been done; consequently, only 74 tumors with accompanying uteri were available. Although this is admittedly a small group, if the original thesis is true, viz., that ovarian tumors may cause irregular uterine bleeding, supporting evidence should appear in a series of this size.

The microscopic sections, gross pathology reports, and the clinical charts were studied in detail. The number of each type of tumor is given in the table.

TABLE I

Pseudomucinous cystadenomas		9
With area resembling serous cystadenoma	2	
With accompanying fibroma	1	
With Brenner tumor	1	
Serous cystadenomas		18
With accompanying fibroma	1	
Serous cystomas		5
With accompanying dermoid	1	
Dermoids		17
Fibroma and fibroadenoma		7
Carcinoma		18

Twenty-seven of the tumors were removed from postmenopausal women. For the purposes of this study a woman was not considered postmenopausal until at least a year had intervened since her last menstrual period. The remaining 47 were considered to be premenopausal although 32 of them were forty years of age.

Findings, Postmenopausal Group

Only four of the 27 patients in this group had postmenopausal bleeding. In two of these patients the bleeding was obviously not due to the tumor per se but to intrauterine pathology. In the third patient, hemorrhagic areas in a hyperplastic endometrium caused bleeding. In the fourth patient, the cause of bleeding could not be definitely determined.

CASE 1.—Was four years postmenopausal. She had a serous cystadenoma, but her bleeding was due to superficial areas of hemorrhagic necrosis in hyperplastic endometrium. The latter as judged by her history was due to the injudicious administration of estrogens during the preceding three years.

CASE 2.—Was 15 years postmenopausal and complained of bleeding for two weeks. Tissue examination revealed a cystadenocarcinoma with metastases to the myometrium. Though serial sections of the small amount of tissue available were searched, no endometrial involvement was demonstrable. A marked hyperplasia present, with numerous hemorrhagic areas was the cause of the bleeding.

CASE 3.—Was a 52-year-old woman who had had no bleeding for seven years following dilatation and curettage and radium for functional bleeding. Prior to admission to

the hospital she had spotted for seven days. At operation, a cystadenocarcinoma was removed along with the uterus. Microscopic preparations of the uterus showed atrophic endometrium with an occasional gland and areas of necrosis covered with fibrin and infiltrated with inflammatory cells. Pyknotic stromal nuclei and other degenerative changes were seen. The bleeding was judged to be due to the intrauterine pathology and not to the ovarian tumor.

CASE 4.—The patient was 59 years old and was 18 years postmenopausal. During the two months prior to admission she bled a small amount at irregular intervals. A papillary serous cystadenoma was removed with the uterus. The endometrium was atrophic but had areas resembling the estrogenic phase of the childbearing period. Such a picture is, of course, not unusual in the postmenopausal period (Novak and Richardson,[15] and Fahlund and Broders[5]). A small fibroid 1.5 cm. in diameter was located just below the endometrium. Unfortunately the gross tissue was not available, and judging from multiple sections, the block had been cut to include only the edge of the tumor. No probable source for the bleeding was found in the available sections, and its cause was not determined.

Premenopausal Group

This group included 47 patients with ovarian tumors. Eleven (28 per cent) of these patients had had abnormally excessive, prolonged, or irregular uterine bleeding. The cause was obvious intrauterine pathology in six patients (endometrial polyps in four; uterine carcinoma in one; submucous fibroid in one). The five remaining cases are described.

CASE 5.—A 37-year-old woman whose history was much too brief, merely a statement that she had had "functional uterine bleeding" prior to surgery. The ovarian tumor was a pseudomucinous cystadenoma. A recent corpus luteum was noted. The endometrium was secretory. Our information on the patient is too scant to make satisfactory evaluation possible.

CASE 6.—The patient was 23 years old. Seven years before, following childbirth, she developed pelvic inflammatory disease. Since that time she had had uterine bleeding every 10 to 15 days for 7 to 10 days. Microscopic examination revealed a serous cystadenoma and residues of pelvic infection. The endometrium was in the proliferative phase but also showed evidence of chronic infection. The onset of the abnormal bleeding immediately following the onset of the pelvic inflammatory disease and the operative findings of the residues of the disease would implicate them as the cause of the bleeding. Though we know of no satisfactory explanation as to the exact mechanism, it is a known clinical fact that abnormal uterine bleeding may be found with residues of pelvic inflammatory disease.

CASE 7.—Following a blow to her abdomen twelve years before, a 37-year-old woman was operated upon. Some unknown ovarian surgery was performed. No tumor was noted but following the operation she bled every 10 to 15 days for 3 to 5 days. The endometrium was in the secretory phase, with no pathology noted. The ovarian tumor was a serous cystadenoma. The bleeding pre-existed the tumor in this patient. It, therefore, seems obvious that the tumor did not cause the bleeding.

CASE 8.—The patient was a 37-year-old woman whose only menstrual irregularity was regular midcyclic spotting for 4 to 5 days during the past year. The ovarian tumor was a dermoid. The endometrium was secretory. This apparently represents the not too rare phenomenon of midcycle spotting associated with ovulation. To attribute the cyclic spotting to the dermoid hardly seems justified.

CASE 9.—A 24-year-old woman with an ovarian fibromyoma, who for the past year had menstruated every 21 days instead of her usual 28, with a two-day flow instead of five. Midcycle spotting was an occasional occurrence. It was noted on her history that the last menstrual period was 26 days previously. The endometrium was in the secretory

phase. It seems rather questionable that we should classify this as abnormal menstruation. One wonders about the accuracy of the history in view of the stated last menstrual interval.

Comment

In 74 pre- and postmenopausal patients fifteen (20 per cent) had abnormal bleeding. In all but three of these patients (Cases 2, 4, and 5) other factors than the ovarian tumor were found which could well explain the bleeding. In one of the three the history was unsatisfactory, merely a statement that the patient had "functional uterine bleeding."

In this study we were not able to find any relationship between the tumors and the endometrial picture. It seems likely that the nonhormonal ovarian neoplasms per se, rarely, if ever, cause abnormal uterine bleeding; furthermore, if adequate study of the pertinent material is done another cause will be found in almost all instances.

Additional Data

The variability in the status of the postmenopausal endometrium was of interest. Less than half (44.4 per cent) showed atrophic endometrium—thin endometrium with scanty glands and low, inactive-appearing epithelium. Approximately a quarter (25.9 per cent) of the endometria had areas of atrophy intermingled with areas where the glands were greater in number, well developed and with high epithelium—areas that resembled the estrogenic phase of a normally cyclic uterus. Two other patients (7.4 per cent) had endometria identical in all respects to that of the normal proliferative phase. The remaining 22 per cent had hyperplastic endometria (excluding the one caused by administered estrogen) but only one of them had been bleeding.

Thus, according to commonly accepted criteria, over half of these postmenopausal women had endometria that showed evidence of estrogenic stimulation. These findings, of course, are not new. Essentially similar findings have been reported by Novak and Richardson, and by Fahlund and Broders.

In none of these postmenopausal patients was there histologic evidence of functional ovarian activity to account for the estrogenic stimulation of the endometrium. In another patient, excluded from this series, such evidence was found. This 46-year-old woman was two years postmenopausal and had had uterine bleeding for five months. The original pathologic diagnosis on her tissues was serous cystoma. Actually, the cyst was a regressing atretic follicle cyst and for this reason she was excluded from this series. Her endometrium was identical to that of the late proliferative phase. Sections of ovarian tissue included a completely normal mature follicle in addition to several small atretic follicles. In this particular instance, the patient had been judged to be postmenopausal because of her history. Actually, judging by the appearance of the ovaries, she had continued to have ovarian activity in spite of the absence of menses.

The findings in this patient cannot be interpreted as support for the theory that on rare occasions postmenopausal uterine bleeding may be caused by a temporary reawakening of ovarian activity. However, this does occur. We have studied the tissues from three such cases. Each of the three patients was at least two years postmenopausal and complaining of uterine bleeding. In each, the ovaries were small, shrunken, inactive, and typical of senile ovaries. In each, however, there was a partially collapsed cystic structure with a wall composed of layers of partially or completely luteinized granulosa and theca cells. The endometria of these patients were hyperplastic and had superficial areas of hemorrhagic necrosis.

It seems likely that these three specimens actually represent instances of reawakening of ovarian activity. Indicative evidence of similar occurrences has been presented by other workers. Cheek and Davis[4] noted secretory endometrium in a woman two years postmenopausal, who had had an episode of bleeding, and no palpable ovarian tumor. Fahlund and Broders noted the presence of a corpus luteum in the ovary of a 63-year-old woman who was 25 years postmenopausal.

Summary and Conclusions

A possible relation between abnormal uterine bleeding and nonhormone-producing ovarian tumors was investigated. Tissues that included uteri as well as the ovarian tumor were available from 74 patients. Abnormal uterine bleeding was not common and in all but three instances definitely could be attributed to causes other than the ovarian tumor. It seems unlikely that nonhormone-producing ovarian tumors, per se, cause abnormal uterine bleeding.

References

1. Adair, F. L., and Watts, R. M.: Am. J. Obst. & Gynec. **34**: 799, 1937.
2. Berkeley, C., White, C., and Cook, F.: Diseases of Women, ed. 7, Baltimore, 1942, Williams and Wilkins Company.
3. Bourne, A., and Williams, L.: Recent Advances in Obstetrics and Gynaecology, ed. 6, Philadelphia, 1945, The Blakiston Company.
4. Cheek, D. B., and Davis, J. E.: Am. J. Obst. & Gynec. **52**: 756, 1946.
5. Fahlund, G. T. R., and Broders, A. C.: Am. J. Obst. & Gynec. **51**: 22, 1946.
6. Fauvet, E.: Arch. f. Gynäk. **159**: 585, 1935.
7. Geist, S. H.: Ovarian Tumors, New York, 1942, Paul B. Hoeber, Inc.
8. Geist, S. H.: Am. J. Obst. & Gynec. **30**: 650, 1935.
9. Koucky, J. D.: Ann. Surg. **81**: 821, 1925.
10. Lippert, W.: Arch. f. Gynäk. **74**: 589, 1904-5.
11. Marwil, T. B., and Beaver, D. C.: Am. J. Obst. & Gynec. **43**: 99, 1942.
12. Mayer, A.: Zentralblatt f. Gynäk. **45**: 345, 1921.
13. Meyer, R.: Zentralblatt f. Gynäk. **49**: 1662, 1925.
14. Moulonguet-Doléris, P.: Gynéc. et Obst. **9**: 493, 1924.
15. Novak, E., and Richardson, E. H.: Am. J. Obst. & Gynec. **42**: 564, 1941.
16. Payne, F. L.: Am. J. Obst. & Gynec. **54**: 762, 1937.
17. Smith, George van S.: Medical Records and Annals, Houston, Tex., July, 1937.
18. Taylor, H. C., and Millen, R.: Am. J. Obst. & Gynec. **36**: 22, 1938.
19. Te Linde, R. W.: Wisconsin M. J. **36**: 521, 1937.

SHEDDING OF DECIDUA DURING UTERINE PREGNANCY AND ITS CLINICAL SIGNIFICANCE

MARY SPIVACK, M.S., M.D., CHICAGO, ILL.

(From the Obstetric Departments of Mount Sinai Hospital and The Chicago Medical School)

DURING pregnancy the uterine mucosa undergoes characteristic changes which are known as decidual reaction. At one time, the decidual transformation was considered the histologic characteristic of the endometrium alone. With the accumulated knowledge it was learned that decidual tissue may be found not only in the endometrium but in the cervix also. Bayer[1] is being credited with the first (1885) demonstration of decidual tissue in the cervix. A number of publications appeared in the literature since then. Some authors described localized elevations or nodules upon the portio vaginalis uteri. Others saw this tissue within the cervical canal or at the external os, appearing as polyps or tumorlike structures. Still others found decidual cells in the cervical erosions. Most of the writers considered their findings unusually rare. While in some cases the occurrence of decidual tissue in the uterine cervix may have only an academic interest, in others it is associated with a symptomatology which might confuse the diagnosis and alter the prognosis of the pregnancy, unless the true nature of the lesion be recognized. The present author's case, which differed essentially from others, emphasizes this point clearly. The tissue in question, found in the cervical canal of an early pregnancy, resembled grossly fetal membranes. This finding aroused fear for the pregnancy itself and raised the question of proper treatment. To emphasize the diagnostic pitfalls and their avoidance is the purpose of this report and its justification.

On Jan. 16, 1947, Mrs. M. L., a 31-year-old white woman presented herself with a history of amenorrhea of ten weeks' duration. Her last menstrual period occurred on Oct. 28, 1946. She complained of a profuse vaginal discharge of long duration, which became especially aggravated during this period of amenorrhea. The discharge was very annoying and irritating, causing rawness and soreness of the perineum.

Her past history revealed a number of childhood diseases. Diphtheria, whooping cough, measles, and mumps were among those she could remember. Her menses began at the age of 14 years. The periods occurred regularly; the flow, moderate in amount, lasted four to five days. There was no history of dysmenorrhea, clots, or other abnormalities. Her past obstetric history revealed that in 1943, after a protracted labor, the patient was delivered of a living child by a midforceps operation. The recovery from the delivery was uneventful. However, the patient dates the onset of the vaginal discharge from the birth of her child. Her family history was negative and irrelevant to the present condition.

The general physical examination of this well-nourished woman was essentially negative except for a systolic murmur at the apex of the heart. A slight contraction of the transverse diameter of the outlet, which measured 9 cm., was the only deviation from normalcy in the pelvic measurements. The pelvic examination disclosed a soft, movable, anteverted uterus, enlarged to the size of about 10 weeks' gestation. The adnexa were not palpable. The cervix was inflamed and badly eroded. A grayish-white membrane was visible within the cervical

canal at the level of its middle third. The origin of its upper extremity could not be determined definitely. There was a profuse yellowish discharge bathing the cervix and vulva. The perineum was found reddened, excoriated in several points, and tender to the touch. The appearance of it gave credence to the patient's statement that the leucorrhea was of long standing. When this strip of membrane was gently touched, slight bleeding occurred, which was easily controlled by pressure. A piece of tissue, measuring 1.5 cm. in length was removed and fixed in 95 per cent alcohol for future study. Grossly, the strip of tissue appeared paper thin, firm, and resembled fetal membranes. After removal of this tissue, another small piece was still visible in the cervical canal. At the second prenatal visit, three days later, it was still present in the upper portion of the cervix. During the following two weeks the patient, according to her statement, was passing small bits of tissue in addition to the fluid vaginal discharge. At the end of this period the author observed the membrane in the patient's cervix for the last time.

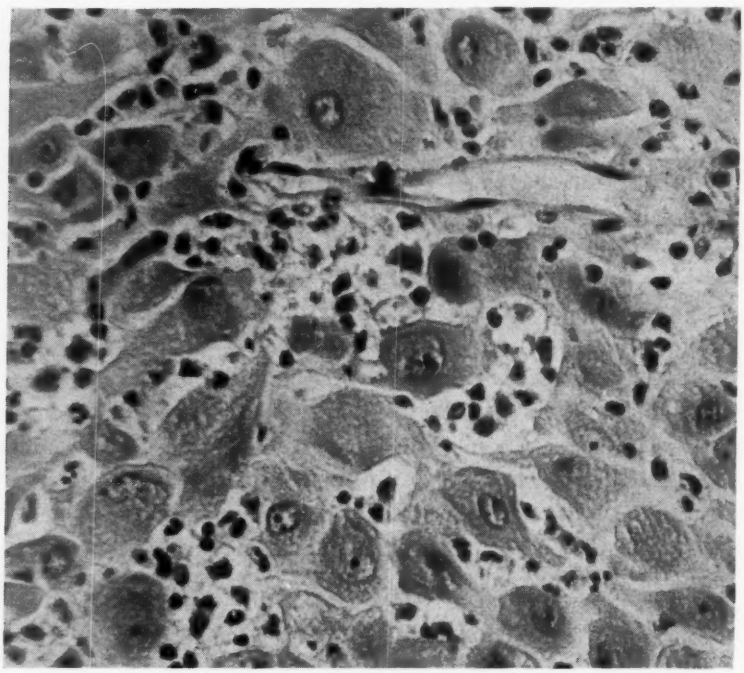


Fig. 1.—Microphotograph of the decidual membrane. This field shows decidual cells with their characteristic vesicular nuclei. The mosaic pattern of the polygonal cells, some of which contain vacuoles, is well illustrated and so is the presence of some caudate forms. Note the large number of polymorphonuclear leucocytes, widely disseminated between the decidual cells. A thin-walled blood vessel is seen in the upper third of the picture. H and E stain, ×400.

The patient complained that on several occasions she had seen small streaks of blood in her vaginal discharge. The bleeding occurred mostly upon exertion, urination, or defecation. The spotting of blood ceased at 7½ months of her pregnancy. The profuse leucorrhea continued throughout its entire period, save for the week just preceding the delivery. The prenatal course was uneventful in every other respect. The blood pressure readings and repeated urinalyses were normal throughout the whole period of gestation. The weight gain and blood count were within normal range. The Kahn test was negative and the patient was free from Neisserian infection. Her blood belonged to group A and was Rh negative, with no antibodies present. Her husband, fortunately, was Rh negative also. The rabbit test (Friedman) was positive for pregnancy.

On July 29, 1947, one week before term, the patient was admitted to the Mount Sinai Hospital in active labor. After a first stage of six and one-half hours and second stage of

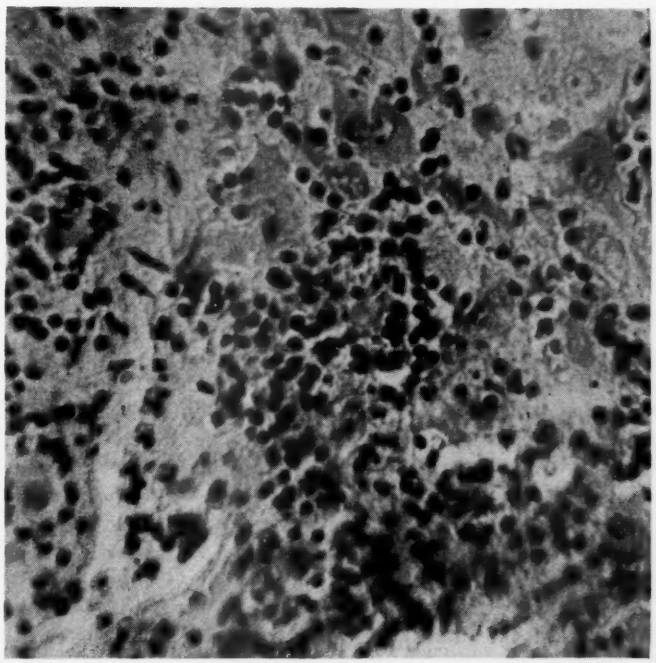


Fig. 2.—Another area of same specimen. This field shows foci of leucocytic infiltrations. Only an occasional decidual cell can be detected here and there. H and E stain, ×400.

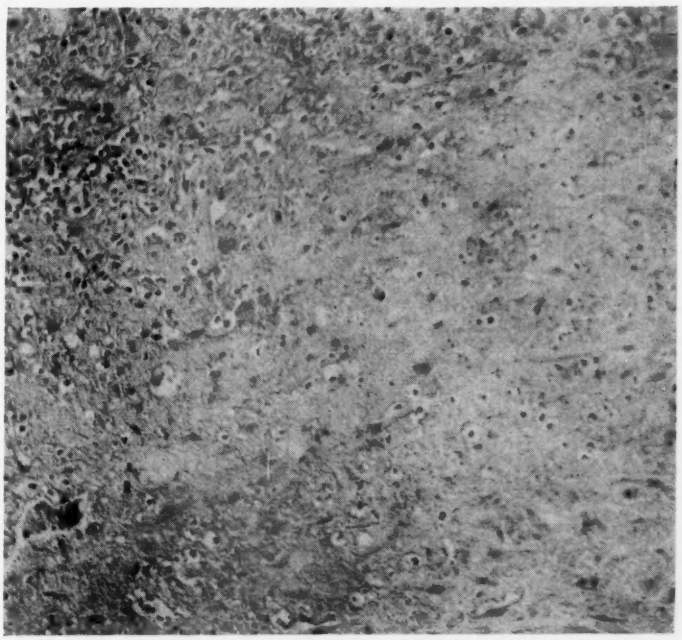


Fig. 3.—An area of necrosis, same specimen. The tissue here appears pale and poorly stained. The decidual cells lost their sharp outline, and they are difficult to recognize, only shadows of them are seen. The leucocytes are numerous even here and have retained to a considerable degree their staining properties. H and E stain, ×180.

one hour, fifty-four minutes, the patient was delivered by low forceps of a normal living child in good condition. The placenta was delivered by early expression after a third stage of four minutes; the loss of blood was estimated at 200 c.c. Careful inspection revealed no abnormalities in the placenta or membranes, which were of usual thickness and smoothness. The puerperium ran an uneventful course, the lochia appeared normal and contained no unusual tissues. There was no morbidity, according to the accepted standards, the highest temperature being 100.2° F. on the evening of the date of delivery. The uterus was involuting satisfactorily. Postnatal examination, at two months post partum, revealed an inflamed and eroded cervix and a well-involuted uterus. The adnexa were not palpable. The vaginal discharge, although diminished in quantity, was profuse still. The pelvic floor was found moderately relaxed and the perineum excoriated still in a few areas.

Microscopic Study of the Specimen.—The major portion of the section consists of decidual cells. These are large, polygonal cells, which vary widely in size. Besides the polygonal, spindle-shaped and caudate forms are seen. The cytoplasm is finely granular and displays vacuoles frequently. The nucleus is vesicular, large, excentrically located and contains coarse granules. Occasionally two nuclei were found in one cell. In some fields the typical mosaic pattern can be observed (Fig. 1), in others edema can be detected. Polymorphonuclear leucocytes are widely disseminated between the decidual cells, in some areas crowding them out completely. In several areas foci of polymorphonuclear leucocytes predominate the field, where they are present almost to the exclusion of any other tissue (Fig. 2). The whole specimen is richly supplied with thin-walled blood vessels of various diameters. There is one large area of necrosis where only shadows of decidual cells can be recognized and few blood vessels detected. Even here leucocytes can be found in large numbers and well stained (Fig. 3). It should be emphasized that the inflammatory infiltration is a striking feature of the microscopic picture.

Discussion

Decidual reaction in the cervix during pregnancy is not nearly as rare as was formerly believed. Decidual or decidua-like cells were repeatedly seen in the cervical stroma by several observers under normal and abnormal conditions (Hofbauer,[8] Novak,[16] Kramann[10]). That decidual reaction to a limited degree does normally occur in the cervical mucosa is accepted by Greenhill in DeLee-Greenhill's[4] "Principles and Practice of Obstetrics." Stander,[20] too, mentions the rare occurrence of isolated decidual cells underneath the cervical epithelium. Since Bayer's[1] publication in 1885, a number of articles were added to the literature. Most of the authors described tumorlike formations within the cervical canal or upon the portio vaginalis. Frequently decidual tissue was found in association with cervical erosions and polyps. Lynch[13] in 1913 collected from the literature twenty-two cases of localized decidual growths in the cervix and added one of his own. Willer,[21] in 1935, assembled seventeen cases of decidual cervical polyps, two of his cases being included in the series. The last decade brought a number of papers upon this subject. Thus, cases were reported by Ostrčil,[17] v. Latzka,[11] Willer,[22] Göbel,[3] Kramann,[10] Hennessy,[6] Klein and Domeier,[9] and Haas.[5] When decidual tissue, well localized and circumscribed, is found either upon the portio or within the two lower thirds of the cervical canal it can be classified as ectopic decidua, since its origin from the endometrium can be positively excluded. On the other hand, considerable more difficulty is encountered when the structure is located in the vicinity of the isthmus. To trace the origin of a tissue in this location is neither easy nor feasible. In the present author's case, the lower edge of the membrane was seen in the middle of the cervical canal. After 1.5 cm. of this tissue had been removed, some more of it was visible at a higher level. Further exploration was omitted for fear of producing hemorrhage difficult to control here, or of endangering the pregnancy. The tissue itself did not contain glands or surface epithelium, the presence of which could have helped in the differential diagnosis.

Histologically, the tissue was identical with the picture seen in the compact layer of decidua vera. Since the mucosa of the isthmus is considered as normally undergoing decidual reaction in pregnancy, decidual tissue in its close vicinity is difficult to classify as ectopic with certainty, unless the whole uterus is available for gross and microscopic study. The present author will refrain from positively identifying the decidua of her case as ectopic, although it may well be that. In the case presented here, the source of the decidua, interesting though it might be, is irrelevant to its clinical importance.

Normally, the endometrium undergoes decidual transformation during pregnancy, and quite naturally this phenomenon was ascribed to the action of the gestational hormones. Outside of pregnancy, decidual reaction of the stroma of the endometrium was observed at times, in cases of polycystic ovaries (v. Latzka[11]), of corpus luteum cysts (Kramann[10]), in luteomas (Novak[16]), and in the premenstrual endometrium in which a decidualike appearance was described (Novak,[16] Curtis,[2] Reinhart,[18] and others), ergo in conditions in which the secretion of corpus luteum hormone is augmented. From the results of his experiments on guinea pigs, Loeb[12] in 1908 postulated that the corpus luteum secretes a substance necessary for development of deciduomas in the animal's uterus, which underwent mechanical stimulation. His views have received wide acceptance and were, subsequently, corroborated by other workers in different species. Nelson and Pfiffner[15] were among the first few to produce experimentally deciduomas in spayed rats by injections of extracts of the corpus luteum, which preceded and followed the mechanical irritation of the uteri. Since then, a number of investigators produced deciduomas in various species by using the progestational hormones in one or another form. These experimental data adduced presumptive support for the clinical chain of evidence which implicates the corpus luteum hormone in the process of decidual formation in man.

Ectopic decidua, by analogy, is also considered a product of corpus luteum hormone stimulation but of nonendometrial tissue. Since ectopic decidua is not a regular finding in every pregnancy, some other factor besides hormonal, must be present for this reaction to occur. Many theories, into discussion of which the author does not intend to enter here, were propagated by various investigators. The theory of R. Meyer[14] that the inflammation, so often accompanying ectopic decidua anywhere in the body, is the sensitizing agent that prepares the susceptible tissues for hormonal response, is of great interest. It seems that this point of view has found corroboration in the histologic picture of many cases of ectopic cervical decidua. In most cases, leucocytic and lymphocytic infiltrations were observed with frequency, almost regularity. In the case presented here, foci of polymorphonuclear leucocytes were a prominent feature of the histologic picture. Even grossly, the cervix appeared inflamed, badly eroded, and exuding a profuse, mucopurulent discharge.

The importance of localized decidual growths, found in the cervix, whether ectopic or not, does not lie in their rarity, but in the fact that their presence might be confused with other, more serious, lesions of the cervix. When located upon the portio or within the cervical canal, these lesions have been mistaken for cancer, tuberculous ulcer, or syphilis. Hinselmann[7] himself failed to make a correct differential diagnosis even with the aid of the colposcope. Careful microscopic studies have been necessary before a correct diagnosis was made in his case. Another point of practical importance is that decidual formations in the cervix may be associated with vaginal bleeding. This bleeding is usually mild but may be profuse and may lead to a faulty diagnosis of placenta previa. Such mistakes have known to occur (Klein and Domeier[9]) and can be prevented by a careful pelvic examination and especially by the use of the vaginal speculum. Cases of bleeding from cervical erosions and polyps, undergoing decidual reaction

during pregnancy, are also known. Once the pathology of the lesion is understood, the problem of treatment becomes simplified. In most cases, the vaginal bleeding is mild and should cause no concern to the attending physician. However, should it be profuse, it can be controlled by pressure or excision or cauterization of the lesion, the pregnancy being left undisturbed. In those cases which had been subjected to biopsy, the healing was prompt and complete. A partial excision of the growth for purposes of study, strangely enough, caused permanent cessation of bleeding for the remainder of the pregnancy (Samuel[19]). An interesting point for speculation is the mechanism of bleeding in cases of cervical decidua. The mere presence of decidual cells, per se, cannot be the cause of it. The great vascularity of the lesion and the tendency to necrosis may furnish a plausible explanation. The removal of friable and necrotic tissue and its substitution by a healthy scar may be a satisfactory explanation for the observation that even biopsies have been able to check the bleeding permanently.

As mentioned already in the case presented here, the tissue, the lower end of which was found in the middle third of the cervical canal, resembled grossly a strip of fetal membranes. In this location, a membranous structure whose upper pole is ill defined can be confused easily with parts of the ovum itself. Its presence here may lead to an erroneous assumption that an abortion is in progress, though pains may be absent. An error like that may be costly to the pregnancy, if one interferes before the microscopic study has been completed. In the author's case, no such action was contemplated because the bleeding had been slight, and the time element was of no great moment. Should a similar macroscopic picture be associated with a more copious bleeding, then the temptation to interfere may be great. Even when the extruded tissue is known to be decidua, another stumbling block may be encountered, unless one is aware of such cases. It is generally accepted that extrauterine pregnancy is accompanied often, although not always, by decidual reaction in the endometrium. The passage of a decidual membrane may not only suggest this diagnosis but also the death of the embryo. A complete history, a careful pelvic examination, the proper interpretation of the Aschheim-Zondek test or any of its modifications, and a discerning evaluation of the symptomatology will be rewarded, in most cases, by a correct diagnosis.

What should the management of such cases be after the diagnosis has been made? In the author's belief, no special treatment is indicated, save for the control of bleeding, if present. This patient was not confined to bed and no special medication was given. At no time, since the nature of the tissue became known, was the pregnancy considered in danger. The patient was allowed her usual activities and continuation of her household duties. Sexual intercourse, however, was interdicted for fear of contact bleeding.

In conclusion, it can be said that if the source of every bleeding in pregnancy be determined, and if the histologic character of every tissue expelled be investigated, then some operative deliveries could be avoided on one hand and some pregnancies salvaged on the other. An accurate diagnosis and knowledge of the underlying pathology are essential for the intelligent management of such cases and indispensable for the acceptance of the old adage, *Primum—non nocere!*

References

1. Bayer, H.: W. A. Freund'schen Gynäk. Klin., 1885 (Quoted from Lynch).
2. Curtis, A.: A Textbook of Gynecology, ed. 5, Philadelphia and London, 1946, W. B. Saunders Company, p. 31.
3. Göbel, A.: Zentralbl. f. Gynäk. **63**: 2317, 1939.
4. Greenhill, J. P.: From DeLee-Greenhill: Principles and Practice of Obstetrics, ed. 9, Philadelphia and London, 1947, W. B. Saunders Company, p. 16.
5. Haas, R.: Am. J. Obst. & Gynec. **54**: 124, 1947.
6. Hennessy, J. P.: Am. J. Obst. & Gynec. **46**: 570, 1943.

7. Hinselmann, H.: Zentralbl. f. Gynäk. **56**: 2406, 1932.
8. Hofbauer, J.: Am J. Obst. & Gynec. **25**: 779, 1933.
9. Klein, J., and Domeier, L.: Am. J. Obst. & Gynec. **51**: 423, 1946.
10. Kramann, H.: Arch. f. Gynäk. **172**: 339, 1941.
11. v. Latzka, A.: Zentralbl. f. Gynäk. **61**: 201, 1937.
12. Loeb, L.: J. A. M. A. **50**: 1897, 1908.
13. Lynch, F.: Surg., Gynec. & Obst. **16**: 694, 1913.
14. Meyer, R.: Ztschr. f. Geburtsh u. Gynäk. **74**: 250, 1913.
15. Nelson, W., and Pfiffner, J.: Proc. Soc. Exper. Biol. & Med. **27**: 863, 1930.
16. Novak, E.: Gynecological and Obstetrical Pathology, ed. 2, Philadelphia and London, 1947, W. B. Saunders Company, pp. 63, 123, 404.
17. Ostrčil, J., Jr.: Zentralbl. f. Gynäk. **60**: 1694, 1936.
18. Reinhart, H.: Am. J. Clin. Path. **5**: 365, 1935.
19. Samuel, M.: Zentralbl. f. Gynäk. **49**: 2893, 1925.
20. Stander, H. J.: Textbook of Obstetrics, 3rd revision, New York and London, 1945, D. Appleton-Century Company, p. 104.
21. Willer, H.: Zentralbl. f. Gynäk. **59**: 979, 1935.
22. Willer, H.: Deutsche. Med. Wchnschr. **64**: 1003, 1938.

A STUDY OF 145 CONSECUTIVE TWIN PREGNANCIES

W. D. Hawker, M.D., and Melvin Allen, M.D., St. Louis, Mo.

(From the Department of Obstetrics and Gynecology, Washington University School of Medicine)

THIS paper represents a study of 145 consecutive sets of twins delivered in the twelve-year period from 1935 to 1947 at the St. Louis City Hospital. During this time there were 15,878 deliveries. The incidence of twinning was 0.91 per cent, or about 1 in 103 deliveries. All of the mothers were white. Das,[1] in his demographic study of twins, showed the incidence among the whites in the United States to be about 1 in 88. This figure is paralleled by Guttmacher,[2] Gernez and Omez,[3] Potter and Crunden[4] and Silbenthal.[5]

Many investigators have already reported the frequency of multiple pregnancy among the multiparas. Only 20 per cent of the twin deliveries in our series occurred among primiparous women. There were 19 sets of identical twins delivered in this study, an incidence of 13.1 per cent. Fraternal twins numbered 126 sets, or 86.9 per cent. Guttmacher[2] noted in his study an incidence of fraternal twins of 93.3 per cent. One hundred fifty, or 51 per cent of the newborn were female. Both sexes were represented in 52 sets, or 35.8 per cent. The sex ratio varied but slightly from the normal expectation.

Prenatal clinics were attended by a minority of the mothers. The burden of multiple pregnancy definitely increased the incidence of toxemia. Twenty-nine and six-tenths per cent of the pregnancies were complicated by a toxemia. Of these 43 cases of toxemia, there were four cases of eclampsia. Polyhydramnios was noted in six of the pregnancies.

The diagnosis of twin pregnancy depends largely upon the size of the babies. The average weight of the twins in this study was 2,420 Gm., with the largest set having a combined weight of 8,060 Gm., or 17 pounds, 12 ounces. Park[6] recently reported a set of twins whose combined birth weight was 19 pounds, 2 ounces.

Other factors, such as obesity, the stage of labor, and the duration of the pregnancy, play an important role in the facility of diagnosis. The diagnosis is not simple, but when suspected can be confirmed by the use of the x-ray. In this series, most of the mothers entered the hospital in active labor. The weights of the babies were fairly equally distributed in three groups. The greatest accuracy in diagnosis was noted in those groups where at least one or both of the babies weighed over 2,500 Gm. The poorest diagnostic ability was demonstrated in the group where both babies weighed less than 2,500 Gm. each. Table I classifies this series according to birth weight and accuracy of diagnosis.

All but two of the deliveries in our study fell in the four common groups of presentation. The incidence of the presentations was roughly identical with the figures usually found by other authors. Table II compares the presentations in this group with that of Leonhardt.[7]

Concern about delivery is due chiefly to the delay incident to uterine inertia, and to a complication known as collision; the latter is exceptionally

rare and was not encountered in this study. The fetal membranes of the second child usually appear at the cervix after the first child is born, and rupture soon follows. The delivery of the second child occurs within a short time of the delivery of the first. In the group under study, 90, or 62.7 per cent, of the second babies delivered within the first 15 minutes, and 123, or 84 per cent, were born within 30 minutes of the first baby; 98.6 per cent delivered within one hour. In only six cases did the birth of the second child occur over an hour after the first. The longest time interval between any two babies was two hours and fifty-three minutes.

Operative interference was frequent in this series. In delivery of the second child, 29 (20 per cent) versions and extractions were performed. There were 21 forceps and episiotomies and one manual rotation of an occiput posterior. Forceps rotation was done in four cases.

TABLE I. DIAGNOSIS AND BIRTH WEIGHT

BIRTH WEIGHT	CASES	PER CENT	DIAGNOSED	NOT DIAGNOSED	PER CENT DIAGNOSED
Both over 2,500 Gm.	56	38	35	21	62.5
Only one over 2,500 Gm.	40	27.5	18	22	45.0
Both under 2,500 Gm.	49	33.9	18	31	36.8
Total	145	100	71	74	49.0

TABLE II. PRESENTATION

PRESENTATION	CASES	INCIDENCE	LEONHARDT'S INCIDENCE
Vertex-vertex	73	49.9	38.5
Vertex-breech	38	26.1	21.2
Breech-vertex	20	13.8	14.4
Breech-breech	12	8.2	10.8
Breech-transverse	1	0.7	4.3
Transverse-vertex	1	0.7	0.8
Total	145	100.0	90.0

TABLE III. INFANT MORTALITY AND MATURITY

MATURITY	CASES	MACERATED STILLBORN	STILL-BORN	NEONATAL DEATH	POST-NEONATAL DEATH	TOTAL DEATHS	CORRECTED DEATH RATES PER CENT
Full-term	155	0	7	5	3	15	3.2
Premature	135	3	5	36	5	49	26.6
Totals	290	3	12	41	8	64	14.1

In the correction of the full-term mortality rates, elimination depends upon the presence of the following conditions:

1. Macerated stillbirths
2. Stillbirths in which fetal heart was not heard prior to labor
3. Postneonatal deaths (after two weeks)
4. Syphilis

In the correction of premature fetal mortality rates, the birth weight of 1,500 Gm. was arbitrarily chosen as the weight of viability.

Of the 148 sets of twins there were 135 premature and 155 full-term infants delivered. There were 15 full-term and 49 premature deaths. The

corrected premature fetal mortality rate was 26.6 per cent, and the corrected full-term fetal mortality rate was 3.2 per cent. This represents a definite increase in the mortality rate for twins as compared to the general obstetric service where the full-term mortality rate was only 1.21 per cent. Table III presents infant mortality and maturity comparisons.

Operative interference was noted to have a corrected mortality rate of 10 per cent. Though this is high, the policy of teaching the technique of versions utilizing the second twin should not be abandoned, for the corrected death rate for that procedure was only 3.47 per cent. The high forceps death rate was due mainly to difficult forceps rotations. Table IV illustrates the

TABLE IV. INFANT MORTALITY AND OPERATIVE INTERFERENCE

OPERATION	CASES	MACERATED STILLBORN	STILL-BORN	NEO-NATAL DEATH	POSTNEO-NATAL DEATH	TOTAL DEATHS	CORRECTED DEATH RATE PER CENT
Versions and extractions	29	1	1	1	1	4	3.4
Forceps and episiotomies	21	2	0	4	2	8	19.0
Total	50	3	1	5	3	12	10.0

mortality rates in those cases in which operative interference was noted.

Among the complications of delivery, the cord was wrapped around the neck of the infant in nine cases. Three prolapsed cords were noted.

The incidence of postpartum hemorrhage was definitely high in this study. Excess blood loss (more than 500 c.c.) occurred in thirteen cases. Hemorrhage caused the one maternal death for an incidence of 0.68 per cent, or 68 per 10,000. Hirst[8] and others have pointed out that in twin pregnancies, maternal, neonatal, and stillbirth rates are roughly increased three times over those for single births. In one instance it was necessary to pack the uterus. In three cases of retained placenta, manual removal was necessary. The tendency toward postpartum hemorrhage is explained on the basis of uterine atony resulting from overdistention by the multiple pregnancy.

Perineal tears were infrequent. There were five first-degree, and seven second-degree tears. There were no third-degree tears. One cervical laceration requiring suture was encountered.

Placental malformations were particularly high. There were two circumvallate placentas and one velamentous insertion of the cord. There were three cases of marginal placenta previa, an incidence of 2.1 per cent. There was only one premature separation of the placenta. The increase in the size of the placenta probably accounts for the increase in the incidence of low-lying placentas.

Five fetal monstrosities were encountered.

Summary

1. A series of 145 consecutive twin deliveries at the St. Louis City Hospital occurring during the last twelve years was analyzed.

2. The incidence of twinning was about 1 in 103 deliveries.

3. In 80 per cent the mothers were multiparas.

4. The incidence of identical twinning was 13.1 per cent.

5. A toxemia complicated the pregnancy in 29.6 per cent.

6. The diagnosis of multiple pregnancy was not easy, especially when both babies weighed less than 2,500 Gm.

7. The presentations varied but little from those presented in the literature.

8. Eighty-four per cent of the second infants were delivered within thirty minutes of the first.

9. Postpartum hemorrhage was encountered in 8.9 per cent of the deliveries and caused the single maternal death for a rate of 68 per 10,000.

10. The maternal, full-term, and premature mortality rates were elevated to about three times that of single pregnancies.

11. Operative interference, especially in the delivery of the second child, should not be abandoned.

12. Placenta previa occurs more frequently in multiple pregnancy.

References

1. Das, Sir Kedamath: J. Obst. and Gynaec. Brit. Emp. **41**: 227, 1934.
2. Guttmacher, Alan F.: AM. J. OBST. & GYNEC. **34**: 76, 1937.
   Ibid.: AM. J. OBST. & GYNEC. **38**: 277, 1939.
3. Gernez, L., and Omez, Y.: Rev. franç. de gynéc. et d'obst. **37**: 916, 1938.
4. Potter, Edith L., and Crunden, A. B.: AM. J. OBST. & GYNEC. **42**: 870, 1941.
5. Silbenthal, R. De: J. A. M. A. **131**: 7, 1946.
6. Park, L. M.: Lancet **246**: 118, 1944.
7. Leonhardt: Ueber die Kindeslagen Bei Zwillingsgeburten. D.I. Berlin, 1897.
8. Hirst, John C.: AM. J. OBST. & GYNEC. **37**: 4, 1939.

16 HAMPTON VILLAGE PLAZA

OBSERVATIONS IN BEHAVIOR OF PRESENTATION AND RESULTS WITH EXTERNAL VERSION IN 190 BREECH CASES*

PAIGE E. THORNHILL, M.D., NORFOLK, VA.

THIS paper will give evidence that 98.4 per cent of spontaneous changes in presentation occur before the thirty-fourth week of pregnancy, that the period between the thirty-second and thirty-fourth weeks is the best time for correcting faulty presentations, and that, for breech delivery, it is the footling type that is most hazardous.

The Kings Daughters Maternity Center in Norfolk, from which eighty-eight of these cases are taken, is an out-patient clinic, from which abnormal cases are referred to a hospital, and normal cases are delivered at home by senior students. The effort to avoid taking complicated cases for home delivery sharpens attention on prenatal diagnosis. From about the thirtieth week, patients are placed on the table at every visit, and presentation and position are recorded. Each is checked at least once by a consultant, and oftener when an abnormality is found. When we are in doubt about presentation, or disagree, x-ray films are ordered. Among these eighty-eight breech cases personally checked, only five were x-rayed.

That the diagnosis of presentation without x-ray may be erroneous is acknowledged. To check on this point one thousand clinic charts were personally examined, to see how the recorded prenatal diagnosis checked with the recorded presentation at delivery. These charts were unselected, except that each had to show the record of at least four prenatal examinations, and the record of presentation as delivered. They did not include the charts of known breech cases separately considered. Three incorrect diagnoses were found; three times I diagnosed "vertex," when it proved to be a breech. A fourth unexpected breech had not been checked by a consultant. So the percentage of error appeared reasonably satisfactory.

In the same one thousand charts, the instances of spontaneous change in presentation after the thirty-second week were also counted, with the following results:

Breech to vertex, or vertex to breech	32nd to 34th week	16
	34th to 36th week	2
	36th to 40th week	2
Transverse to upright	32nd to 34th week	0
	34th to 36th week	1
	36th to 40th week	2

Only seven changed after the thirty-fourth week, less than 1 per cent.

*Read at the Tenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Augusta, Ga., Feb. 12 to 14, 1948.

In our breech group of 190 cases, the percentage of change after the thirty-fourth week was found to be higher, for no apparent cause:

Vertex to breech	35th week	5
	36th week	4
	37th week	1
	38th week	2
		12

So the combined groups, totaling 1,190 cases, showed that only 19 spontaneously changed presentation after the thirty-fourth week, which is 1.6 per cent. This corresponds closely to the findings of Weisman[1] who followed 100 unselected cases by x-ray.

If spontaneous change mainly ceases at the thirty-fourth week, the preceding fortnight should be the optimum time for correcting faults. Siegel[3] gives the thirty-second to the thirty-sixth week as the best time for external version.

Unlike presentation, position changes frequently, right up to term.

In analyzing the breech group, we counted as a breech every case found in breech presentation after the thirty-second week, omitting multiple pregnancies. The series includes the fifty-eight cases reported to the Virginia State Society in 1935.

In general, it is our policy to try to correct all faulty presentations by the thirty-fourth week of pregnancy. Before the thirty-second week, our experience indicates that spontaneous change is so common that interference is impracticable. Within this two-week period, thirty-two to thirty-four weeks, the baby appears small enough to be turned with fair ease, yet large enough to maintain its presentation when turned.

The technique of external version is extremely simple. When presentation and position have been definitely determined, with aid of x-ray when there is doubt, the most important requisite is gentleness. Abdominal muscles must be relaxed. Then slight but steady pressure applied to the poles in the right direction carries the buttocks upward and the head forward and downward in increased flexion.

Before taking up the 160 successfully turned, let us note a few things about the 30 that were not turned:

Breech Cases That Were Not Turned

Correctly diagnosed, external version tried and failed			25
Wrongly diagnosed, and no version attempted			5
Proved to be	Footlings	2	
	Full breech	3	
	Frank breech	16	
	Type unrecorded	9	
			30

Of this last 9, the records show that one was a cesarean, 8 were spontaneous except for episiotomies, and all babies lived. So, for reasons given later, it seems fair to assume that most of them were of frank type. At any rate, the predominance of frank breeches among the cases where external version failed, was pronounced.

Longest labor, 27 hours. Frank breech, 10 pound baby.

Infant mortality, one. Full breech decomposed, 9½ pound baby; probably a section should have been done for disproportion.

That the frank breech is definitely the most difficult to turn, is in accord with the findings of Ryder,[2] Siegel and McNally,[3] and Watson.[4] The extended

legs on upturned thighs constitute an effectual splint to the entire body, so the flexion necessary for turning cannot be obtained.

But, fortunately, this is the type of breech that is least troublesome, and least dangerous. The ease with which a frank breech often delivers may give a false sense of security about breech deliveries in general. The baby sits squarely over the cervix, the buttocks making an effectual stopper against cord prolapse, while the cervix is sufficiently dilated by the combined diameters of the baby's pelvis and thighs. I wish to emphasize the importance of these combined diameters, for complete cervical dilatation. Birth may be entirely spontaneous.

Now let us consider the group successfully turned:

VERSION SUCCESSFUL IN 160 OF 190 CASES, OR 84 PER CENT

When done	30th to 32nd week		7	
	32nd to 36th week		119	
	36th to 40th week		34	(4 were turned during labor)
			160	
Required a second turning		19		
Required a third turning		5		
Required a fourth turning		0		
Resulted in spontaneous vertex delivery				133
Forceps delivery				19
Podalic version for prolapsed cord				1
Cesarean section				7
				160
Complications:				
Persistent occipitoposterior			8	
Face or brow presentation			0	
Prolapsed cord			1	
Other cord complications			0	
Premature separation of placenta			0	
Labor induced by version			0	
Weight of babies:				
Over nine pounds			27	
Between eight and nine pounds			40	
Less than five pounds			1	
Babies delivered as vertex and lost			3	

1. Mother chronic nephritic; 9½ pound baby; difficulty in extracting shoulders; death from birth injury.
2. Died 40 hours before delivery; intrauterine *Cl. Welchii* infection; mother survived; reported in 1945.
3. Macerated; fetal heartbeat absent from one week prior to a single version.

Infant mortality:
In 190 cases, four, or 2 per cent.
If corrected by omitting cases 2 and 3 above, the rate would be 1 per cent.

Maternal mortality 0

In counting spontaneous deliveries, episiotomies were not considered as operative interference. A forceps delivery means some degree of dystocia.

Attention is called to the absence of cord complications. It is our belief that, in doing an external version, one is avoiding cord complications, rather than inviting it, because we are substituting a single pole, the head, for a double pole, the feet. Surely, the double pole is the more liable to entanglements.

Gentleness in manipulation is believed to account for the absence of placental disturbance and induction of labor. Strenuous effort is unwise and unnecessary. Anesthesia is dangerous.

In further reference to the delivery of breech cases, it is my belief that 90 per cent of the difficulties with breech births in general occur with footlings, either as primary footlings, or because another type was converted into a footling by operative means. With no disproportion, serious trouble threatens from one of two things, prolapse of the cord, or incomplete dilatation of the cervix. Both are major complications.

When a foot or leg is below the buttocks at the onset of labor, the irregular shape and small size of the presenting part causes early rupture of membranes, and allows space for the cord to work down; the cervix has such an irregular cork, or stopper, that the cord can easily prolapse; and cervical dilatation proves insufficient, because the baby's pelvis and thighs came through it separately.

In my opinion, this is a clear indication for a dilating bag. If, when the cervix is open 2 to 3 cm., a No. 6 Voorhees bag is introduced, it will hold back both cord and legs until dilatation is sufficient for quick and safe delivery. Nothing smaller than a No. 6 bag should be used. Effort is made to keep membranes intact, a two-pound weight is attached, and Demerol and scopolamin are given freely. Kosmak[5] and Irving and Goethals[6] employ bags for "selected" cases of breech labor, but they do not specify for which particular type.

For the same reason, when one brings down the legs of a full or frank breech, a comparatively safe type is converted into a dangerous type. We need to be more cautious about decomposing to speed delivery, as pointed out by Gordon, Garlick, and Oginz,[7] Ware, Winn, and Schelin,[8] Bill,[9] Hansen,[10] and Guyer and Heaton.[11] Gordon, in a study of three thousand breech deliveries, demonstrated that interference with normal mechanism, and rapid extraction, is the real cause for fatal outcome in many cases. I confess I am not able to tell, always, whether a cervix is completely dilated and paralyzed, or not. Trouble with the cervix has been encountered, when dilatation was thought to be absolutely complete. Goethals,[12] who, with Irving, advocated decomposition at full cervical dilatation, reported a fetal mortality of 5 per cent.

We need to think, and consider very carefully, before proceeding with decomposition. Fearing disproportion, in spite of negative x-ray evidence, we develop impatience and an urge to do something. But unless the baby or mother shows distress, it appears safer to allow more than the traditional two hours in second-stage labor, relieving pain by analgesics, and giving supportive intravenous treatment as indicated. We need to think more about the advantage of those upturned thighs in the mechanism of labor. The advantage is real.

Summary

One thousand unselected charts and the records of one hundred ninety breech cases indicate that in 98 per cent of cases the fetus has assumed its final presentation by the thirty-fourth week of pregnancy.

External version is a safe and easy maneuver.

The optimum time for version is between the thirty-second and thirty-fourth weeks.

In a series of 190 breech cases, version was successful in 84 per cent, with an uncorrected fetal mortality of 2 per cent.

Failures were mostly due to the extended legs of the frank breech.

In labor, the footling is far more hazardous than the other types; for it, we recommend the early use of a large dilating bag, as a safety measure.

The frank and full breech types are most safely delivered by conservative management, simple episiotomy and assistance to shoulders and head after the baby is half born.

In every case coming to delivery as a breech, x-ray determination of the exact type is highly important. The type of breech, as well as the relative size, must be known at the onset of labor, for safe management.

References

1. Weisman, A. I.: Am. J. Obst. & Gynec. **48**: 550, 1944.
2. Ryder, G. H.: Am. J. Obst. & Gynec. **45**: 1004, 1943.
3. Siegel, I. A., and McNally, H. B.: Am. J. Obst. & Gynec. **37**: 86, 1939.
4. Watson, P. M.: Am. J. Obst. & Gynec. **45**: 1020, 1943.
5. Kosmak, G. W.: Am. J. Obst. & Gynec. **45**: 1020, 1943.
6. Irving, F. C., and Goethals, T. R.: Am. J. Obst. & Gynec. **11**: 86, 1926.
7. Gordon, C. A., Garlick, R., and Oginz, P.: Am. J. Obst. & Gynec. **28**: 140, 1934.
8. Ware, H. H., Winn, W. C., and Schelin, S. C.: Am. J. Obst. & Gynec. **54**: 748, 1946.
9. Bill, A. H.: Am. J. Obst. & Gynec. **49**: 574, 1945.
10. Hansen, E. M.: Am. J. Obst. & Gynec. **41**: 575, 1941.
11. Guyer, H. B., and Heaton, C. E.: Am. J. Obst. & Gynec. **52**: 362, 1946.
12. Goethals, T. R.: Surg., Gynec. & Obst. **70**: 620, 1940.

QUADRUPLET PREGNANCY: DIAGNOSIS AT SEVENTEEN WEEKS OF GESTATION*

J. WILEY HARTMAN, JR., M.D., FRANK FEIGHTNER, M.D., AND PAUL TITUS, M.D.

(From the Latrobe General Hospital, Latrobe, Pa., and the John C. Oliver Memorial Research Foundation, St. Margaret Memorial Hospital)

THIS instance of quadruplet pregnancy merits reporting notably because it appears to be the earliest positive diagnosis on record. The diagnosis was established by a combination of clinical observations and x-ray studies, seventeen weeks after the first day of the patient's last preceding menstrual period. The case was successfully concluded at approximately thirty-one weeks by the delivery by cesarean section of living quadruplets, one male and three females, apparently being the second on record of delivery by section.[1]

Multiple pregnancy was tentatively diagnosed by Dr. Hartman, when palpation during the early weeks of pregnancy showed excessive uterine enlargement. The patient's last menstrual period began on July 12, 1947. Nearing the seventeenth week the fundus of the uterus was slightly below the level of the lowest ribs, and she was referred by Dr. Hartman for x-ray on Nov. 7, 1947, exactly seventeen weeks from the first day of the last menstruation. Dr. Feightner's report is quoted verbatim: "Anteroposterior and lateral radiographic examination of the abdomen reveals the presence of four fetal skulls and vertebral columns in this abdomen. These fetuses are of approximately five months' gestation. The height of the fundus is at the lower border of the first lumbar vertebra. No other abnormalities are noted."

The anteroposterior film is reproduced herewith without retouching, but the diagnostic points are, regrettably, much less evident than in the original film seen in a viewing box. This is understandable, however, because the centers of ossification of a fetus are usually not clearly visible until about the eighteenth week, or the middle of a pregnancy.

Subsequent x-rays taken on Dec. 31, 1947, and Jan. 30, 1948, distinctly show the quadruplets and their relative positions.

On Feb. 14, 1948, namely, at thirty and one-half weeks from the beginning of the last period, the patient's membranes ruptured spontaneously, and a few hours later mild uterine contractions began.

A secondary trachelorrhaphy had been done on this patient in 1946, three years after her first pregnancy and delivery in 1943. It had been decided in an antenatal consultation, however, to subject her to a test of labor in this present delivery because the cervix seemed soft. After about seven hours of weak labor pains, the cervix was dilated to a stiff, sharp-edged ring about 3 cm. in diameter without progressive increase for several of these hours. On the indications of long-ruptured membranes (fourteen hours), primary uterine inertia, and cervical dystocia from scar tissue, cesarean section was performed by Dr. Titus, using the lower uterine segment (Kerr-Phaneuf technique) type of section.

The first infant, the male, had a single, separate placenta; the other three (females) had a single large placenta with separate amniotic sacs and a single chorion.

All were vigorous, though small (each slightly more than 3 pounds, or 1,361 Gm.) and obviously premature. All have survived to date and are growing well. They have been given repeated pediatric consultations by Dr. Richard R. O'Toole of Pittsburgh.

The patient's recovery was uneventful.

---

*Presented before the Pittsburgh Obstetrical and Gynecological Society, April 5, 1948.

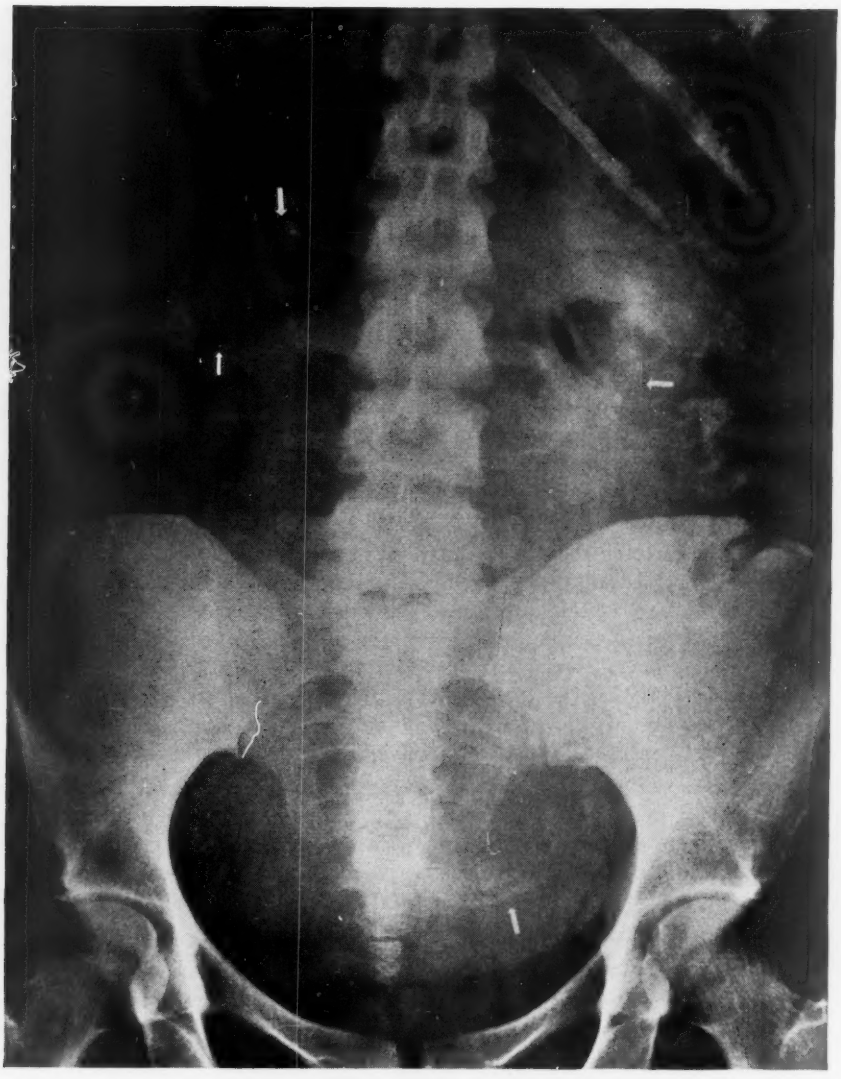


Fig. 1.—X-ray at 17 weeks' establishing early diagnosis of quadruplets. The long bones and spines are more visible than the skulls.

Summary

1. Quadruplet pregnancy occurs about once in 550,000 pregnancies.

2. This case reported was correctly diagnosed at approximately 17 weeks of gestation, by a combination of clinical and x-ray findings, apparently the earliest diagnosis on record.

3. Delivery of small, premature infants of a multiple pregnancy can usually be accomplished through the pelvic canal. Uterine inertia and cervical dystocia from postoperative scar tissue necessitated delivery by cesarean section in this case, apparently the second on record.

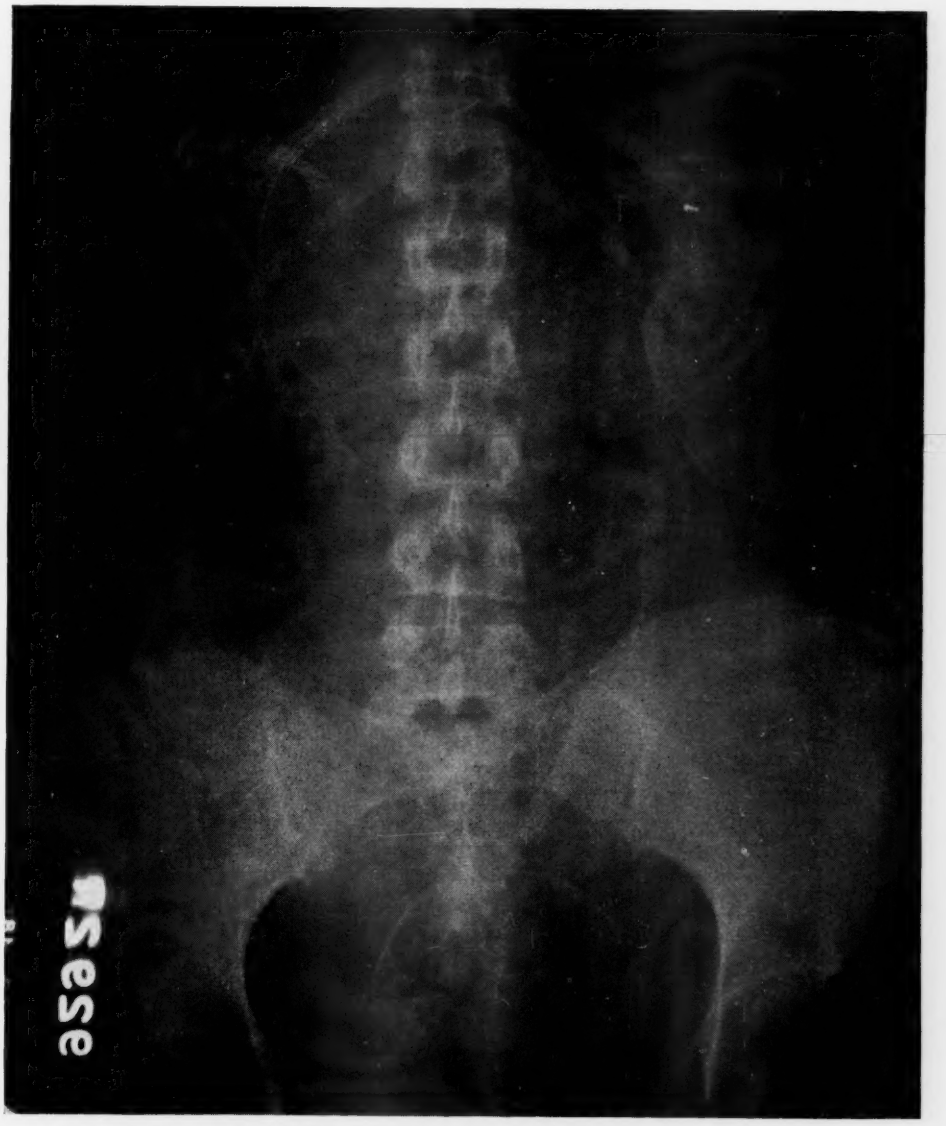


Fig. 2.—X-ray of quadruplet pregnancy at about twenty-eight weeks.

4. The survival rate of quadruplets is low. These infants are living and thriving. They were under incubator care for their first several weeks of life.

5. The pregnancy consisted of a single fetus (male), and identical triplets (females).

Reference

1. Ullery, J. C.: J. A. M. A. **128**: 183, 1945.

A RUPTURED ABDOMINAL PREGNANCY WITH MASSIVE, RAPID TRANSFUSIONS AND UNCOMPLICATED RECOVERY

SYDNEY LURIA, M.D., BALTIMORE, MD.

(From the Departments of Obstetrics and Gynecology, Sinai Hospital)

THE great amount of blood given to this one patient, and the rapidity of its administration, impelled us to report this case. The survey of recent literature, including studies conducted during World War II, reveals no instance of an individual surviving after being given 7,500 c.c. of whole blood within a six-hour period.[2-6] It is axiomatic that, in general, severe blood loss must be replaced at a rate dependent upon the speed of hemorrhage. Practically the only exceptions are cases with pulmonary or intestinal injuries.

Case History

G. C., a 25-year-old, para 11001, was first seen at the Sinai Obstetrical Clinic Sept. 9, 1947. Records later obtained from the Baltimore City Hospital stated that the patient was seen by them in this same pregnancy May 28, 1947, when she gave the history of spotting associated with crampy lower abdominal pains on April 1, May 8, and May 28. Her last menstrual period was Jan. 20, 1947, and the estimated date of confinement Oct. 27, 1947. Obstetric history revealed that she had had an uneventful breech delivery of a seven pound, two ounce infant at another hospital in 1941. Examination, September 9, also showed a breech presentation, blood pressure 98/60, and hemoglobin 74 per cent. The patient was given a return appointment for September 30, but on September 25, at 9:30 A.M., the husband called to state that his wife was having severe abdominal pain following a gentle bump. He had slipped on a crayon and the point of his elbow collided with his wife's abdomen. This was immediately followed by pain of such severity that she could not move. Patient was brought by ambulance to the accident room at 10:30 A.M. She was in obvious shock and complained of severe abdominal pain, worse in the right upper quadrant. Her blood pressure was 70/50, pulse 130. The upper abdomen was tense, more markedly so on the right; pressure in the right upper quadrant caused severe pain. The lower abdomen was comparatively soft, and an irregular area in the region of the umbilicus could be made out. Percussion elicited dullness in both flanks. The fetal heart was heard to the left of the umbilicus. Because of the rigidity of the abdomen, small parts could not be palpated. A diagnosis of ruptured uterus was made by the resident obstetric staff, the patient was cross-matched with Rh-positive, type A blood, and a 500 c.c. transfusion was started immediately. A consultant from the senior staff confirmed the diagnosis and the patient was immediately taken to the operating room where, under cyclopropane anesthesia, the abdomen was opened through a right rectus incision. The peritoneum was tense and discolored; when it was incised, approximately 1,500 c.c. of blood and clots escaped. The fetus was found lying free in the peritoneal cavity and was easily delivered. The cord which was very short was torn from its attachment to the placenta by this manipulation. Examination revealed that the uterus was intact, soft, and enlarged to approximately a three to four months' pregnancy. The placenta and membranes were attached to the right adnexa below, omentum above, parietal peritoneum to the right and laterally, and it was believed at this time that there was an attachment to the intestines posteriorly. It was decided not to disturb the placenta and a 4 inch rent, situated to the left and anteriorly through which the baby had been extruded from the sac at the time of its rupture into the abdominal cavity, was sutured. Hemostasis was reinforced by placing Oxycel gauze over this sutured tear in the placenta. As the peritoneum was being closed, an ooze of bright red blood was noticed in the right gutter. The exact site of this bleeding was not determined but it was believed to be from a slight separation of the placenta during delivery of the baby. This region was packed with Oxycel gauze but complete hemostasis was not obtained. The abdomen was then closed with the belief that the Oxycel gauze and a tight binder would control oozing. The 4

pound, 11 ounce baby girl lived for four hours and post mortem revealed atelectasis with no other abnormalities except facial deformity. Suter and Wichser[12] found that 38.7 per cent of living viable babies in extrauterine pregnancies were deformed and 24.3 per cent of the babies died before the eighth day. They quoted Winckel as stating that 75 per cent of all deformed children had abnormalities of the head. Following operation, the patient's pulse which had been unobtainable became discernible but was too rapid and weak to be counted. Blood pressure was 70/50 at this time. Nasal oxygen was started, and blood and plasma were given under syringe pressure through cutdowns in both arms. Despite the eight bottles of whole blood (the first three, group A crossmatched, the remainder group O unmatched) and 750 c.c. of plasma, the patient again went into deep shock. Blood pressure and pulse were unobtainable, red blood cells 3.05 millions, hemoglobin 10.7 Gm. (73 per cent), hematocrit 32. The abdomen was distended, tense, and dull to percussion. It was felt that the patient was hemorrhaging internally and the abdomen was reopened through the old incision at 2:45 P.M. (two and one-half hours after the first closure) under light gas-oxygen anesthesia. Approximately 2,000 c.c. of blood and clots were removed from the peritoneal cavity and a bleeding area the size of a dime was found on the right posterior margin of the placenta. This area was the site of active hemorrhage. The placenta and membranes were delivered through the abdominal wound and, as they were not attached to the intestines, clamps were placed across the omental attachment above, and the right Fallopian tube below. These attachments were cut and sutured. The raw area in the right gutter was packed with Oxycel gauze, the abdomen closed with through-and-through silver wire, and the skin with interrupted black silk sutures. During this procedure and immediately postoperatively, an additional seven bottles of whole blood (six, group O unmatched, one, group A crossmatched) and 500 c.c. of plasma were administered. Patient had a slight chill at this time. At 6:00 P.M., the blood pressure was 120/80, pulse 140, temperature 103.6° F., red blood cells 3.4 millions, hemoglobin 15.8 Gm. (106 per cent), hematocrit 47. The patient was taken to her room and placed in an oxygen tent and a Miller-Abbott tube inserted. Penicillin, 75,000 units every three hours and a course of Prostigmine were ordered. During the next twenty-four hours, sixteen ampules of sodium lactate were administered. The latter was given in glucose, in distilled water, and in normal saline. She was also given Parenamine, and vitamins at the same time. Urinary output during the first seven postoperative hours was 1,500+ c.c. (via retention catheter); the urine was alkaline, containing 5 to 10 red blood cells per high power field.

	2ND DAY	3RD DAY	5TH DAY	7TH DAY	11TH DAY	12TH DAY
Output (c.c.)	4,140+	2,950	1,200+			
Intake (c.c.)	5,000	3,260	3,320			
Red blood cells	4.85	3.85	4.15			4.7
Hemoglobin	14(97%)	11.3(77%)	12.5(86%)		16(108%)	14(96%)
Hematocrit	40	38	40		47	
Urea	14	15	18	24		
Uric acid	2.4			3.6		
Chlorides	560	610		568		
Total protein	5.0			5.8	7.7	7.2
Carbon dioxide	52.3			37.4		
Icterus index	2.5					
V.D.B.	0					

The patient was given fluids (with Miller-Abbott tube clamped) on morning of September 27 (40 hours postoperative), which she retained. The Miller-Abbott tube was withdrawn that same morning. Blood pressure maintained at 115/70 and pulse came down to 80 on September 26. The temperature returned to normal on September 27. Oxygen was stopped at this time and the patient placed on a soft diet with no distention present. Aside from a fear of impending death, the patient's convalescence was entirely uneventful, and she was allowed out of bed on September 30 (sixth postoperative day). On October 2, the black silk sutures were removed and the wound looked clean at that time although there was slight

irritation around the silver wire. All medication was discontinued at this time. On October 9, silver wires were removed and the wound was healing by primary union. Patient was discharged the following day (fifteen days postoperative) in good condition. As seen from the case history, except for a slight chill and fever immediately following the last (fifteenth) transfusion, there were no other signs of a hemolytic or pyrogenic reaction.

We should like to consider the amount of sodium citrate injected. Lewisohn, after experimentation on dogs in 1915, concluded that 15 Gm. to a man would be fatal, but since this pioneer work, his dosage limit has often been safely exceeded.[11] There have been reported as much as 5,600 c.c. of citrated blood over a period of forty-eight hours. Our patient, a 52 Kg (115 pound) woman, received 7,500 c.c. of citrated blood in a six hour period with little or no reaction. The exact action of sodium citrate is not known but it is believed that the sodium citrate forms a complex soluble salt (with calcium) which liberates very few calcium ions. Bruneau and Graham[11] have shown the toxic effects of sodium citrate to vary with the dosage and repetition of a certain dose, with the rate of administration, with different animal species, and even with different members of the species. To duplicate their experimental conditions, a man weighing 70 Kg. (154 pounds) would have to be given 6,300 c.c. of blood containing 0.6 per cent citrate within a few hours before a fatal outcome could be expected. This is equivalent to 37.8 Gm. of citrate. In each 500 c.c. bottle given to our patient there was 75 c.c. of anticoagulant containing 2.2 per cent sodium citrate and 0.8 per cent citric acid. Ultimate concentration was 0.33 per cent sodium citrate and 0.12 per cent citric acid. Therefore, 7,500 c.c. of whole blood contained 24.75 Gm. of sodium citrate and 9 Gm. of citric acid.

It is interesting to note that the blood loss in this case was greater than 100 per cent. According to the Ashby method,[3] one bottle of blood forty-eight hours after administration corresponds to a cell volume of 2.8 per cent (350,000 red blood cells per cubic millimeter). The patient's count at forty-eight hours showed:

Total red cell count	3,850,000
Transfused red cell count	5,250,000
Cell volume of patient	38 per cent
Allowance for 15 bottles of blood	42 per cent

Summary

1. Patient received 7,500 c.c. of whole blood in a six-hour period which attests the value of an efficiently functioning blood bank.

2. Rapidity of administration can be easily accomplished by a syringe and a three-way stopcock.

3. Group O Rh-positive blood has a low titer (1-200 or less) of Anti-A and/or anti-B agglutinins and hemolysins.

4. Citrate has low toxicity, a 52 Kg. woman tolerating 33.75 Gm.

5. Active and proper therapy aids in the establishment and maintenance of kidney function post transfusion.

References

1. Sheldon, T. H., Lundy, T. S., and Adams, R. C.: Anesthesiology **7:** 122-131, 1946.
2. Whitby, Sir Lionel: J. Roy. Army M. Corps **85:** 266-270, 1945.
3. Dacie, J. V., and Homer, G. F.: The Lancet **1:** 371-377, 1946.
4. Smith, O. F.: Multiple Transfusions, Rhode Island M. J. **29:** 107, 1946.
5. Dill, L. V., and Murphy, C. J., Jr.: M. Ann. District of Columbia **15:** 214-216, 1946.
6. Tisdall, L. H., et al.: Am. J. Clin. Path. **16:** 193-206, 1946.
7. Weiner, A. S.: Am. J. Clin. Path. **16:** 233-243, 1946.
8. Crook, C. E., et al.: Surg., Gynec. & Obst. **82:** 417-423, 1946.
9. Muirhead, E. E., et al.: Surg., Gynec. & Obst. **82:** 405-413, 1946.
10. Moloney, William C.: Brit. M. J. **2:** 916-918, 1945.
11. Bruneau, T., and Graham, E. A.: Arch. Surg. **47:** 319-325, 1943.
12. Suter, M., and Wichser, C.: Am. J. Obst. & Gynec. **55:** 489-496, 1948.

SPONTANEOUS RUPTURE OF A PRIMARY CARCINOMA OF THE OVARY COMPLICATING PREGNANCY

AUGUST DARO, M.D., CLAIR M. CAREY, M.D., AND BRUCE P. ZUMMO, M.D.,
CHICAGO, ILL.

(From the Departments of Obstetrics, Cook County Hospital and University of Illinois School of Medicine)

PRIMARY malignancy of the ovary complicating pregnancy is uncommon. Case reports are conspicuously few in the literature. It has been stated by Szathmary[9] that 5 to 7 per cent of ovarian tumors associated with pregnancy are malignant. Traut and Kuder reported 53 ovarian tumors in 2,300 deliveries. Two were malignant; an incidence of 3.7 per cent.[11] At the Cook County Hospital, this is the only recorded proved case since 1932.

In 1942 Brossert presented fifteen authentic cases.[12] His summary failed to include cases reported by Danforth and Greenhill.[7, 8] In 1933, Van Szathmary stated that he had found thirty-nine cases in world literature, of which seven were sarcomas and thirty-two were carcinomas.[9] Most of these cases, however, were obtained from various clinical tabulations of ovarian tumors. In most instances authenticity of the malignancies, in the presence of pregnancy, was not verified by microscopic study.

We wish to present a case, and to add to the official list the following cases: Wells (1882), Casati (1883), and Murphy (1895), as revealed by Swan in 1898.[1] We feel that the case of Hempel, which was evidently a bilateral Krukenberg ovarian tumor secondary to carcinoma of the stomach, should not be included in the list of primary ovarian malignancy complicating pregnancy. This brings the total number of authentic reports to nineteen.

Case Report

B. H., a 24-year-old Negro woman, gravida iii, para ii, was admitted to Cook County Hospital on July 10, 1947, in the service of Dr. Daro. Her last period had occured on Oct. 3, 1946. She attended prenatal clinics of the Infant Welfare Society. Their initial examination on Feb. 2, 1947, showed no pelvic pathology.

Her complaints on admission were: abdominal cramps for two days, fainting and weakness for the past five hours. Pregnancy had been uneventful until two days prior to admission, when she noted the onset of lower abdominal discomfort. The pain was intermittent and mild at first, but became more frequent, severe, and diffuse. About five hours prior to admission, the pain suddenly became sharp, and the patient felt weak and faint. Her abdomen began to feel "bloated." She was seen by physicians from the Chicago Maternity Center. They found her in shock, with a blood pressure of 70/40, gave plasma and stimulants, and sent her to Cook County Hospital.

Physical examination on entrance revealed an acutely ill Negro woman, manifesting mild dyspnea and beads of perspiration on her forehead. Her blood pressure was 90/60, temperature 97° F., and respirations 28. The skin was cold and clammy; the conjunctivae and oral mucosa were pale. Lungs were clear and resonant. Abdomen was distended, tense, and tympanitic. Liver, kidney, and spleen were not palpable. Peristaltic sounds were absent. Fundus of the uterus extended two finger breadths above the umbilicus. Corpus felt firm, tense, and somewhat tender to palpation. Fetal sounds were not made out. External genitals were negative, with no evidence of fresh or old blood. Clinical impression was: abruptio placenta, or possible ruptured uterus. Urine was negative for sugar, acetone, and albumin.

*Presented before the Chicago Gynecological Society, Feb. 20, 1948.

Red blood cells 2.8, hemoglobin 39 per cent, white blood cells 15,600. Five hundred cubic centimeters of plasma and 500 c.c. of whole diluted blood were started in both arms. During surgery another 500 c.c. of blood were given.

When the abdomen was opened under ether and nitrous oxide anesthesia, the peritoneal cavity was filled with fresh and old blood, and much soft, mushy, brainlike material. The uterus was the size of six and one-half to seven months' gestation, and intact. A large, ruptured, left ovarian cyst was delivered with frayed margins. The right ovary contained a corpus luteum of pregnancy. The impression was that of a unilateral, ruptured, malignant ovarian tumor. Owing to the patient's critical condition, only a salpingo-oophorectomy was done, and the abdomen was closed immediately.

Pathology report by Alex B. Ragins, M.D. "Specimen of ovary presented a morcellated appearance, the largest fragment measuring 15 by 9 by 2 centimeters. The free surface was light purplish-gray, smooth, and appeared to be part of a cyst filled with soft, putty-like material. Microscopic section of ovary revealed a very anaplastic undifferentiated carcinoma of the ovary with a tendency to form glandlike structures."

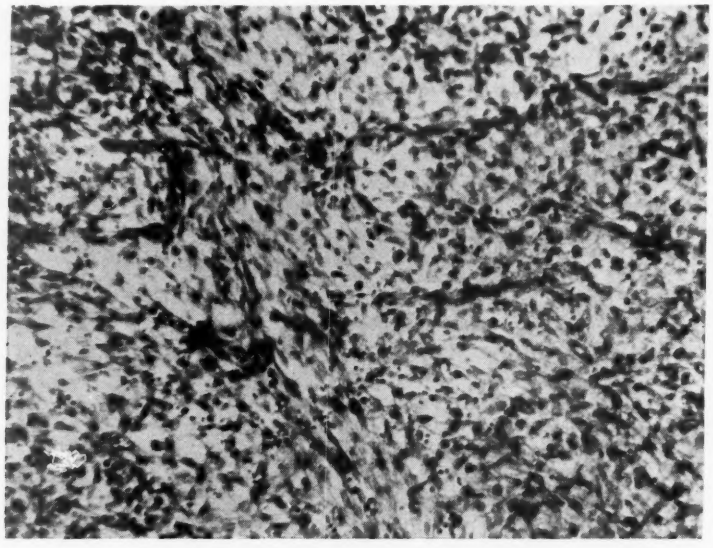


Fig. 1.—Ovarian tissue revealing a very anaplastic undifferentiated carcinoma, with tendency to form glandlike structures.

Her postoperative course was uneventful. Ten days later, x-ray therapy was started. It was decided to give the patient a full course of therapy before further surgery was contemplated. Twenty-five days postoperatively, she went into labor and passed a macerated fetus of about six and one-half months' development. The patient received 250 r. (in air) through eight portals, for a total of 3240 r. per portal. Subsequently she refused further surgery and hospitalization. We had planned to do a total hysterectomy and a right salpingo-oophorectomy. According to the relatives, the patient is now in Jackson, Mississippi, and is reported to feel perfectly well.

Summary

1. Primary ovarian malignancy complicating pregnancy is uncommon.

2. Nineteen authentic cases are reported in the literature; of these nine are sarcomas, the remainder being carcinomas.

3. That herewith reported is the only case of ruptured ovarian malignancy associated with pregnancy.

4. Ruptured ovarian malignancy may simulate abruptio placenta, ruptured uterus, and the other conditions associated with pregnancy causing an acute abdomen.

References

1. Swan, W. E.: Johns Hopkins Hosp. Bull. **9**: 56, 1898.
2. Winckel, F. V.: Handbuch der Geburtshülfe, Munich, 1906.
3. Bumm, E.: Grundriss Zum Studium der Geburtshülfe, quoted by Brossert.[12]
4. Kosmak, G. W.: Am. J. Obst. **70**: 1021, 1914.
5. Zickel: Zentralbl. f. Gynäk. **31**: 385, 1907.
6. Szymanowicz, J.: Gynéc. et obst. **6**: 405, 1922.
7. Danforth, W. C.: Am. J. Obst. & Gynec. **24**: 455, 1932.
8. Greenhill, J. P.: Am. J. Obst. & Gynec. **24**: 789, 1932.
9. Szathmary, Z. V.: Ztschr. f. Geburtsh. u. Gynäk. **106**: 238, 1933.
10. Trillat, P., and Puthod, A.: Gynéc. et obst. **29**: 513, 1934.
11. Traut, H. F., and Kuder, A.: Internat. Clin. **3**: 285, 1940.
12. Brossert, L. J.: Am. J. Obst. & Gynec. **44**: 336, 1942.

30 North Michigan Avenue

DYSGERMINOMA OVARII*

EDWARD S. BURGE, M.D., EVANSTON, ILL.

THE following two cases were seen with Dr. E. L. McGill and Dr. J. L. Hagan, respectively, at the St. Francis Hospital in Evanston, Ill., and it is with their courteous consent that this report is made. Both cases are of dysgerminoma ovarii, or, as they are sometimes called, seminomas. In each case, repeated strongly positive Aschheim-Zondek and/or Friedman tests were obtained. The majority of the literature, including textbooks dealing with dysgerminoma ovarii, describe these tumors as incapable of producing demonstrable changes in hormone balance.

The first case was that of a 23-year-old nun, first seen in August, 1939. She complained of having had intermittent left abdominal pain for six years, and then for the past year of an almost constant aching pain in her left abdomen. She had noticed her abdomen becoming larger. One year previous to admission she had had amenorrhea for four months; since then menses had been characterized only by irregularity. The only significant physical finding was a symmetrical firm abdominal tumor rising from the pelvis to 5 cm. above the umbilicus. There were no breast changes. X-rays of the abdomen were negative for fetal structures. The Aschheim-Zondek test was strongly positive on three occasions prior to operation. At the operation a grey-pink, rubbery, smooth tumor replacing the right ovary was removed. Its greatest diameters were 19 by 22 by 13 cm., and its weight 2.1 kilograms. The rest of the pelvis was apparently normal, and the recovery was uneventful. Fourteen days postoperatively an Aschheim-Zondek test was negative, and in March, 1947, seven and one-half years after surgery, the patient was reported to be alive and well.

The second case was similar and first seen in September, 1946. The patient was 23 years old, unmarried, and had always been in good health. She had bled vaginally for three weeks in May, 1946, and had been told that she was very anemic. In June, 1946, she had an apparently normal menstrual period, then amenorrhea for thirteen weeks preceding admission. For about six months she had noticed that her lower abdomen was enlarging, and the only significant finding on physical examination was a symmetrical midline, nontender, tumor mass extending out of the pelvis to 3 cm. above the umbilicus. There were no breast changes, and x-rays of the abdomen were negative for fetal structures. Repeated Aschheim-Zondek tests were strongly positive in two laboratories, and Friedman tests were likewise positive in a third laboratory. At operation a grayish-purple left ovarian tumor of rubbery consistency measuring 18 by 20 by 14 cm. was removed. The other pelvic structures appeared and felt normal. Cut sections of the tumor were gray to gray-pink, with a few streaks and spots of yellow. There was only one cystic area, 2½ cm. in diameter. The patient's recovery was uneventful. Aschheim-Zondek tests done on the tenth and thirtieth day postoperatively were both negative, and a Friedman test done on the fourteenth postoperative day was negative. To date the patient is in good health.

In summary, then, two cases of dysgerminova ovarii were associated with strongly positive "pregnancy tests;" these reactions became negative after the ovarian tumors were removed. The incidence of malignancy in these tumors has been reported as high as 30 per cent. Both of these patients are living and well, one more than seven and one-half years after surgery.

636 CHURCH STREET

*Presented before the Chicago Gynecological Society, March 21, 1947.

MENINGITIS AND MENINGISMUS AS COMPLICATIONS FOLLOWING CONTINUOUS CAUDAL ANESTHESIA

JACOB S. BEILLY, M.D., F.A.C.S., AND SIDNEY J. PECK, M.D., BROOKLYN, N. Y.

(From the Department of Obstetrics and Gynecology, Beth-El Hospital)

SINCE Hingson and Edwards[1-4] first published their experience with employment of continuous caudal anesthesia during labor and delivery, the number of cases similarly treated has steadily increased. More than 200,000 cases have been compiled.[5] The complications noted have been indeed few and meningitis following successful therapy would seem to occur but rarely. The occurrence of meningitis as a complication following caudal anesthesia has appeared in reports of three cases[6, 7, 8] which have been published to date.

Our experience at Beth-El Hospital deals with approximately 7,500 parturient cases. Reports of 250 cases[9] and 2,300[10] cases, respectively, have been published. Following successful therapy with caudal anesthesia of more than 6,000 parturients, several cases of meningeal complications were encountered. A résumé of these and a case report of one of the meningitis patients follows.

1. *Meningitis.*—There were two cases of meningitis as complications following the administration of caudal anesthesia. These cases were dissimilar only as to the severity of the clinical course and duration of illness. Both cases presented spinal fluid findings as increased spinal fluid pressure and cytology predominantly polymorphonuclear leucocytes. However, no bacterial agent was discovered; the smears and cultures were negative. Recovery was complete in both instances.

The first case had a relatively mild course and was discharged in good condition on the seventh postpartum day.

The second case is detailed: A. S. is a 27-year-old, white, para i, gravida ii, who was admitted to the hospital Aug. 21, 1947, in active labor. Temperature 98.6° F., pulse 80, respiration 20, blood pressure 112/70, urinalysis negative.

Continuous caudal anesthesia was administered for one hour and thirty minutes; 60 c.c. of 1.5 per cent Metycaine solution was used. Labor was uneventful. She was delivered of a 7 pound, 1 ounce living male child with low forceps and episiotomy. The total duration of labor was thirteen hours.

Headache and projectile vomiting developed three hours later; shortly following this there was nuchal rigidity and hyperactive deep reflexes; Kernig and Brudzinski signs were positive, bilaterally. She had twitching of the orbicularis oculi and levator palpebrae muscles. Six hours following delivery she was disoriented, became incontinent and comatose. Clonic convulsive seizures recurred during the several hours which followed. Generalized muscular flaccidity appeared and the deep reflexes disappeared. Coma persisted throughout the second postpartum day and her condition improved by the end of that day. Consciousness returned and she began to utter sounds; speech was in monosyllables. Improvement continued gradually and by the end of the sixth postpartum day she became alert, responded to questions, and possessed memory of recent events. Subsequently she improved more rapidly; her memory of remote events returned. The patient became cooperative and by the thirteenth day she recovered completely, being neurologically negative with a normal spinal fluid. On the fourteenth postpartum day she was discharged.

The febrile reaction during the early part of the illness was marked. The temperature rose steadily to 106.2° F. on the second postpartum day. With improvement which followed by the third day it remitted to 103.4° F. and gradually fell to 101° F. on the sixth day, becoming normal and remaining flat the remainder of her postpartum course. Pulse and respiration followed closely changes in temperature.

The spinal fluid was removed under increased pressure. It appeared cloudy with 4,048 cells, 95 per cent polymorphonuclear leucocytes and 5 per cent lymphocytes with 91 mg. per cent sugar. A repeat examination of the spinal fluid at the end of the first postpartum day still showed increased pressure and cloudiness with 5,900 cells, 95 per cent polymorphonuclear leucocytes, 5 per cent lymphocytes with less than 10 mg. per cent sugar and 191 mg. per cent total proteins.

Smears and cultures remained negative. No bacterial agent was recovered by culture at the end of the fourth day.

On the first day of the illness 100,000 units penicillin were administered intrathecally and 50,000 units were given every 3 hours intramuscularly, with 2 Gm. sulfadiazene intravenously every 4 hours.

Fifty c.c. of 50 per cent intravenous glucose and later 1,000 c.c. of 5 per cent glucose in normal saline were given with the sodium sulfadiazene. On the following day 3,000 c.c. of 5 per cent glucose in Ringer's lactate solution were administered.

Sedatives as sodium Amytal were employed occasionally to induce sleep.

2. *Meningismus.*—Shortly after the appearance of the latter case of meningitis there were fifteen parturients who developed symptoms of meningeal irritation following therapy with caudal anesthesia. Duration of anesthesia ranged from 55 minutes to 135 minutes, 45 c.c. to 85 c.c. of 1.5 per cent Metycaine solution being administered. These cases appeared within a twenty-four-hour period and presented varying degrees of meningismus. Few of them complained of headache; more than half of them had nuchal rigidity and hyperactive deep reflexes, and in all of them a positive Kernig sign was illicited. Temperature remained normal throughout the postpartum course; symptoms and signs began to disappear after the second postpartum day. All recovered promptly without sequelae and were discharged on the seventh postpartum day.

The spinal fluid of one of this group was removed without pressure. The fluid was clear with 200 cells, 95 per cent polymorphonuclear leucocytes. Smear and culture were negative.

Discussion

The anesthetic drug employed was 1.5 per cent Metycaine solution. This was made up from ampules by the hospital anesthetist. However, after the fifteen cases appeared with the syndrome of meningeal irritation, the Metycaine solution has been supplied by Eli Lilly & Co. in containers ready for use in each case. More than 1,000 cases have been handled since this change without recurrence of these complications.

There was no evidence to indicate an inadvertent penetration of the anesthetic solution into the subarachnoid space in all of the foregoing cases.

Summary

1. The meningeal complications following successful therapy with continuous caudal anesthesia are summarized.

2. Two cases of meningitis, one of which is reported herein, were encountered. Recovery without sequelae followed in both instances.

3. The syndrome of meningismus of varying degree, typical of a group of fifteen cases, was presented in brief.

Acknowledgment is hereby given to Dr. Abraham Koplowitz for his advice and cooperation and to Dr. Harry Warwick for his kindness in contributing his case of meningitis.

References

1. Edwards, W. B., and Hingson, R. A.: Am. J. Surg. **57**: 459-464, 1942.
2. Hingson, R. A., and Edwards, W. B.: Anesth. & Analg. **21**: 301-311, 1942.
3. Hingson, R. A., and Edwards, W. B.: J. A. M. A. **121**: 225-229, 1943.
4. Hingson, R. A., and Edwards, W. B.: Anesthesiology **4**: 181-196, 1943.
5. Hingson, R. A.: S. Clin. North America **25**: 1352-1381, 1945.
6. Manalan, S. A.: J. Indiana M. A. **35**: 564-565, 1942.
7. Hodges, W. R.: J. A. M. A. **125**: 336-341, 1944.
8. Brown, W. W., Jr.: Am. J. Obst. & Gynec. **53**: 682-683, 1947.
9. Levine, W., Herzlich, J., Halperin, J., and Taller, H.: Am. J. Surg. **64**: 31-39, 1944.
10. Levine, W., Taller, H., and Light, A.: Am. J. Surg. **72**: 47-51, 1946.

901 St. Marks Avenue

THE USE OF AN ESTROGENIC CREAM IN THE TREATMENT OF SENILE VAGINITIS

CHARLES M. MCLANE, M.D., NEW YORK, N. Y.

(From the Department of Obstetrics and Gynecology, Cornell University Medical School, and the New York Hospital)

VULVOVAGINITIS, atrophic vaginitis or senile vaginitis—atrophic conditions of the vaginal mucous membrane usually associated with hypo-estrinism—has long been a therapeutic puzzle. Atrophy may be present in normal postmenopausal women without causing symptoms. However, when a condition or conditions such as itching, burning, dyspareunia, vaginal discharge, and an acute inflammation develop, the discomfort of the patient is often very marked. It has been known that estrogenic hormones given by injection or by mouth may relieve these symptoms, but often the dosage must be pushed so high that irregular or withdrawal bleeding may result. The use of an estrogen in a cream base, applied topically in the vagina by means of an applicator containing .446 mg. of dienestrol when full, has been reported by A. E. Rakoff, M.D. ("A Clinical Evaluation of Dienestrol, a Synthetic Estrogen," *J. Clin. Endocrinol.*, October, 1947) to help cure this condition without producing detectable side effects.

In the course of this study the new potent estrogen, dienestrol, in a cream base,* was given to every patient in the Gynecological Out-Patient Clinic of the New York Hospital who complained of symptoms associated with senile vaginitis, unless there was indication of specific infection or disease. Although a large number of patients received this medication, only 123 have had sufficient follow-up at the present time to be reported here.

At the time of her first visit, each patient was given one tube of cream, instructed to use, every night, one applicatorful (4.46 Gm. of cream containing 0.446 mg. of dienestrol) and to return to the Clinic in one, two, or four weeks, depending upon the severity of the condition. If there was a four-week interval between visits, the cream was used up several days before her return visit. Some patients were subjectively and objectively cured in one or two weeks, and no more cream was given, but usually a second tube was necessary even though the improvement was apparent. All patients were examined at each visit. Vinegar douches were prescribed only when one of the complaints was that of a discharge. If the patient had a recurrence after discontinuing the cream, she was told to resume its use only as frequently as necessary to prevent discomfort, which usually meant once or twice a week. No complications were noted, even in those patients who used the cream irregularly for as long as twelve months. One patient, whose symptoms had improved, developed a definite rash two weeks after beginning treatment, but this disappeared when the cream was discontinued. There were no other reactions noted. One patient, aged 60, who was improving, showed some irregular uterine bleeding after using the cream daily for several months, but this subsided when the amount of cream was reduced to one-third applicatorful daily.

In the 123 cases, 84, or 68.3 per cent, were definitely improved both subjectively and objectively, or were cured; 31 cases, or 25.2 per cent, were classed

*The estrogenic cream (Dienestrol Cream) used in this study was supplied by the Ortho Pharmaceutical Corporation, Raritan, N. J.

as unimproved because they showed either no clinical improvement or were symptomatically no better. However, many of these patients were better either clinically or symptomatically than when they were first seen. In 2 cases, or 1.6 per cent, the condition was aggravated and 6 cases, or 4.9 per cent, could not be evaluated because of other complications such as trichomonas or monilia infections which developed after dienestrol therapy was begun, or because the patients were given oral estrogenic therapy for menopausal symptoms soon after this treatment was started.

We were particularly interested in 80 of the total number of cases who returned to the Clinic in from one to four weeks after receiving the estrogenic cream. The complaints of these 80 were as follows: itching, 36; discharge, 29; burning, 17; spotting, 7; dyspareunia, 8; with some patients presenting more than one complaint. The diagnoses made were: senile vaginitis in 63 cases; pruritis vulvae, 3; leucoplakia, 5; kraurosis, 1; and others such as vulvovaginitis, vulvitis, and traumatic vaginitis in 17; some cases having more than one diagnosis. We have divided these 80 as follows:

	CONDITION		
FOLLOW-UP IN	IMPROVEMENT	NO IMPROVEMENT	AGGRAVATED
1 week	8	4	1
2 weeks	26	7	0
3 or 4 weeks	25	9	0
Total	59	20	1

The 43 remaining patients, of whom six were eliminated as explained previously, did not return until after at least four months and of these, twenty-five were improved, eleven unimproved, one worse.

The cream was used also on two children having a nonspecific vaginitis, one aged 6 and the other 10 years. In both cases the discharge cleared up very promptly and did not recur. However, because of the possible unpleasant complications associated with vaginal manipulation in children, we believe that some other form of therapy is preferable.

Although previously it had been thought that an estrogenic cream was contraindicated in leucoplakia, dienestrol in a cream base was prescribed for five such cases only as a means of controlling the extreme itching and excoriation, with quick and excellent results in four cases.

Summary

In this investigation 123 patients received dienestrol in a cream base for the treatment of atrophic changes occurring in the vaginal mucosa. All of these patients, with the exception of two children and two adults, were over 40 years of age. In 68.3 per cent of the cases, after receiving this type of therapy, the vaginal mucosa appeared healthy and the patients had no complaints. Those patients who returned to the Clinic at the end of one week of treatment showed rapid improvement. Although 25.2 per cent of the cases were classified as unimproved, it must be noted that some of this group showed either symptomatic or clinical improvement. Relief of symptoms had to be accompanied by clinical response before the patient was considered improved. Further topical application of the estrogenic cream was prescribed if symptoms recurred. The average healthy vagina was maintained in some instances by using dienestrol one to three times a week over a period of months. No untoward effects were noted.

33 East 68th Street

SPONTANEOUS RUPTURE OF A NORMAL UTERUS ASSOCIATED WITH PLACENTA ACCRETA FORMING A CENTRAL PLACENTA PREVIA

CLAUDE G. CALLENDER, M.D., AND EDWARD L. KING, M.D., NEW ORLEANS, LA.

(From the Departments of Gynecology and Obstetrics, The Tulane University of Louisiana School of Medicine, and Charity Hospital)

THE spontaneous rupture of a normal uterus before the onset of labor is an exceedingly rare obstetrical emergency. Generally speaking, the incidence of rupture of the uterus varies from one in 95 (Whitacre and Lang, Peiping Union Medical College*) to one in 3,029 (Dugger, County of Philadelphia, Pennsylvania, 1945). A figure of one in 2,000 approaches the average reported.

Mrs. M. D. A., a white woman, aged 30 years, was admitted to the Charity Hospital at New Orleans on Jan. 6, 1947, at 3:30 P.M. Her last menstrual period was March 5, 1946, and expected date of confinement, Dec. 12, 1946. Her only other pregnancy eight years before terminated in a difficult breech delivery after a forty-eight hour labor, followed by postpartum hemorrhage, manual removal of the placenta, and morbidity which persisted for one week. No surgical procedures and no abortions, spontaneous or induced, were admitted.

The present pregnancy, under the supervision of her family physician, had been uneventful except for a few days' hospitalization at the sixth month for vaginal bleeding which subsided with bed rest and progesterone.

On the evening before admission the patient noted mild lower abdominal cramps which were not sufficient to keep her awake. She was awakened, however, at 3 A.M. with a moderately severe constant abdominal pain. She entered the local hospital at 7 A.M., at which time her physician saw her. After three to four hours during which several examinations revealed no progress in labor, the pain became much more intense and flat plate of the abdomen revealed the fetus in a transverse position. She was then sent to New Orleans by ambulance. No sedatives and no oxytocics were given. A slight amount of vaginal bleeding occurred en route.

Physical examination on admission revealed an acutely ill, markedly obese woman in profound shock. The blood pressure was unobtainable and the pulse 150. The abdomen was somewhat distended, and the lightest palpation caused the patient to react violently. The remainder of the examination was negative except for a pallor of the palms, nail beds, and mucous membranes.

The blood pressure rose to 120/90 shortly after a transfusion of whole blood was Begun. Vaginal examination disclosed a long hard cervix admitting one finger to the internal os. No presenting part could be felt through the lower segment. No vaginal bleeding occurred. An x-ray plate of the abdomen revealed the fetus in a transverse lie, with the head on the mother's right.

Catheterized urine on admission showed 2 plus albumin, sugar negative. Sediment contained granular casts and 10 to 20 white blood cells per high power field. The admission hemoglobin was 10.5 Gm. The Kline and Kolmer tests were negative.

A tentative diagnosis of rupture of the uterus versus premature separation of the placenta with concealed hemorrhage was made and the patient was laparotomized under ethylene and ether anesthesia. A second and a third transfusion were given during the operation. A

*The incidence of pelvic deformities associated with osteomalacia and the prevalence of untrained midwives is held accountable for these figures.

Fig. 1.—Specimen as seen from above.

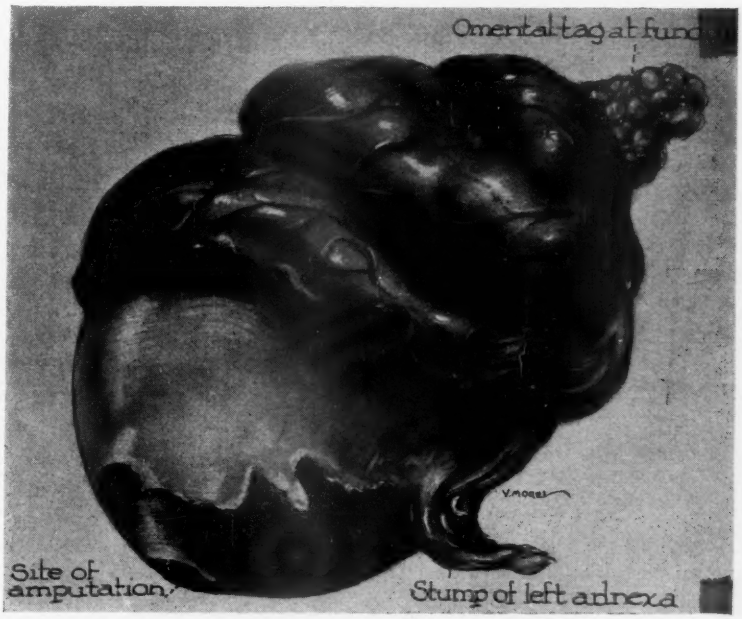


Fig. 2.—Drawing of lateral view of specimen.

midline subumbilical incision was made and when the peritoneum was opened the cavity was seen to be filled with blood and the dead fetus was lying free in the upper abdomen. The rent in the uterus was transverse across the fundus from one cornu to the other. The placenta was still attached and occupied the position of a true placenta previa centralis. The uterus was firmly contracted. An omental adhesion was noted on the posterior aspect of the fundus. After removal of the fetus, a subtotal hysterectomy was done with the placenta in situ.

Subsequent microscopic section through the site of placental attachment revealed chorionic villi deeply invading the uterine myometrium—a placenta increta (Irving and Hertig).

Convalescence was marked by temperature elevation to as high as 101° F. to the fifth postoperative day and a moderate ileus for forty-eight hours. Penicillin, 50,000 units every 3 hours, had been started just prior to operation. The patient was discharged on the eighth postoperative day, and has been seen twice in the postpartum clinic and is in excellent health.

Summary

An unusual case report is presented in which spontaneous rupture of an apparently normal uterus occurred in conjunction with a placenta accreta which formed a central placenta previa. The mother recovered. The only clues as to previous uterine trauma were the history of a long hard breech delivery, and the finding of an omental adhesion near the site of the rupture. No oxytocic drugs had been administered.

MYASTHENIA GRAVIS COMPLICATED BY PREGNANCY*

CHARLES E. GALLOWAY, M.D., EVANSTON, ILL.

THIS is only the second case of myasthenia gravis complicated by pregnancy which we have had in the history of the Evanston Hospital.

The patient, Mrs. J. M. C., aged 27 years, para i, was sent to me by Dr. L. Blakeman of Chicago. This patient was also seen in consultation a few years ago by Professor Veit of Harvard. The weakness complained of most is that in the right arm and leg. The patient is 5 feet 6 inches tall, and when first seen, 7 months pregnant, she weighed 169 pounds. Her average weight, however, is 155. Her only medical history was that of an appendectomy at the age of 17 and a pilonidal cyst removed at the age of 16 years. Diagnosis of myasthenia gravis was first made in 1944. There was no anemia in this case, the lowest blood count being hemoglobin of 81 per cent and red blood cells 3,840,000. This patient, as stated before, when first seen weighed 169, but just before delivery she had lost 3 pounds and the weight at that time was 166. There was no evidence of any toxemia. The patient was Rh negative and married to a husband who was Rh positive. When first seen, this patient was taking a routine dose of Prostigmine but was unable to walk at any one time more than two blocks. She could start out from her home and by stopping frequently she could walk to the end of the block in which she lived, rest a while, and return to her apartment. She was also unable to do housework for any length of time. She could, by resting frequently, not become too fatigued after she had attempted some simple housework.

She went into labor on Sept. 4, 1947, at about 9 A.M. and by 11 A.M. was having strong, four-minute pains. By 2 P.M. the pains were every two minutes and quite normal in strength and character. At 7 P.M., however, she had only 2 cm. dilatation. At that time her pulse was 105, her eyelids were drooping, she found it very difficult to swallow and speak and her respirations had increased. Due to the fear of a respiratory collapse, it was deemed advisable to terminate the labor. This was then done under local anesthesia at 8:30 P.M. after approximately eleven hours of labor.

During her labor she received Seconal, grains 1½, at 11:15 A.M. At 4:50 P.M., we started 1,000 c.c. of 5 per cent glucose in water. At 4:50 P.M. she received another ampule of Prostigmine and at 4:30 P.M. she was given 50 mg. of Demerol. At 7:15 P.M., prior to operation, she was given scopolamine, $\frac{1}{150}$ grain. The bag of waters was intact and the delivery was effected under a local 1 per cent procaine anesthetic. After delivery, she was given Prostigmine 1-2000, 1 c.c. twice a day and aspirin and codeine for pain. She found it possible to enter into about the same amount of activity following operation as the average patient, except that her periods out of bed were somewhat shortened as she would become short of breath and unduly fatigued. She left the hospital on the twelfth postpartum day and at home is still using Prostigmine. She was last seen on March 8, 1948, and at that time could care for her baby to some extent, but was somewhat confined to the house except for special occasions.

*Presented before The Chicago Gynecological Society, March 19, 1948.

HEMORRHAGE FROM A RUPTURED VARICOSITY IN THE PLACENTA WITH DELIVERY OF A LIVING FETUS

HENRY C. FRECH, M.D., F.A.C.S., SAVANNAH, GA.

(From the Warren A. Candler Hospital)

THERE is only one mention of this condition in a textbook[1] and only two similar cases have been reported.[2, 3] The fetus was lost in both of the latter.

Mrs. M. C. D., aged 19 years, married six months. She became pregnant in April, 1947. Her expected date was calculated to be around Jan. 11, 1948. She had a normal antepartum period.

On Dec. 25, 1947, she was admitted to the hospital in labor at 11:30 A.M. Her pains were regular at intervals of five minutes lasting thirty to forty-five seconds. Her condition was good. The fetal heart tones, 120, were heard in the right lower quadrant. Blood pressure was 120/80; urinalysis was negative. She progressed normally and at 3 A.M. on Dec. 26, 1947, she was taken to the delivery room, with the cervix completely dilated. The membranes were intact and bulging through the labia, the head was on the perineum, the rectum was bulging. At 3:25 A.M. the membranes ruptured spontaneously and there was a gush of bright red blood from the vagina.

A low forceps delivery was immediately performed and a living male infant weighing five pounds, three ounces was delivered at 3:30 A.M., followed by a large gush of grossly bloody amniotic fluid when the body of the baby was delivered. The placenta was expressed in about three or four minutes. There were just a few small clots and a little fresh bleeding. The placenta was of moderate size, well developed, and showed no evidence of retroplacental hemorrhage nor infarcts. There was no evidence of placenta previa marginalis. The cord was attached a little off the center, was of moderate length, and showed no abnormalities.

Examination of the fetal surface of the placenta showed several patches of ecchymosis under the amnion. Closer inspection revealed a small opening on the fetal surface of the placenta, which evidently was the site from which the hemorrhage had occurred. The lesion was a rupture of a small varicosity about 4 mm. in diameter, located about 4 cm. from the periphery on the fetal surface of the placenta.

The hemorrhage was entirely fetal, none of it was coming from the mother. In Leff's case[3] the membranes ruptured six hours previous to the delivery and the child was stillborn. Rannenberg's case[2] resulted in a delivery of a stillborn fetus.

As Leff states, "What to do at the time of the hemorrhage is the problem to decide." Placenta previa and extensive separation of the placenta must be ruled out. If the fetus is dead and the mother is in good condition interference is not warranted. If the hemorrhage occurs when the cervix is not dilated, the fetus would probably be dead before a cesarean section could be done. In this case it was fortunate that the cervix was fully dilated, the baby small, and the forceps were ready for routinely lifting the head over the perineum in a primipara.

Rupture of a velamentous cord resembles this condition and two such cases have been reported by Kosmak.[4, 5]

References

1. Curtis, A. H.: Obstetrics and Gynecology, Philadelphia, 1933, W. B. Saunders Company, vol. 1, page 496.
2. Rannenberg, Elly: Zentralbl. f. Gynäk. **48**: 30, 1924.
3. Leff, M.: AM. J. OBST. & GYNEC. **22**: 117, 1931.
4. Kosmak, Geo. W. AM. J. OBST. & GYNEC. **4**: 619, 1922.
5. Kosmak, Geo. W.: AM. J. OBST. & GYNEC. **16**: 438, 1928.

Department of Reviews and Abstracts

Selected Abstracts

Abortion

Whitacre, Frank E., Hingson, Robert A., and Turner, Henry B.: The Treatment of Eclampsia by Means of Regional Nerve Block, South. M. J., page 920, Oct., 1948.

The clinical and pathological evidence supports the concept that eclampsia is the result of angiospasm. The electro-encephalographic tracings taken during convulsive seizures are typical of those induced by anoxia which in the case of the eclamptic results in angiospasm. The pressor substances probably originate in the placenta.

Regional nerve block controls the hypertension and convulsions of eclampsia through sedation and vasodilatation. This is followed by increased renal circulation which favors an increase in urinary output, reduces blood pressure, and thus relieves the cardiac load. This in turn prevents pulmonary edema, the most common avenue of exit for the eclamptic. The absence of severe narcosis in babies is an important factor in evaluating the regional nerve block in the treatment of eclampsia. Regional anesthesia is induced by continuous caudal administration of a 1.5 per cent solution of Metycaine in a dose of one to two c.c. each hour. Anesthesia is maintained throughout labor and the results have been gratifying.

WILLIAM BICKERS.

Kriseman, M. M.: Intrauterine Penicillin, Edinburgh M. J., page 293, May, 1948.

The author reports seven cases of incomplete abortion, one case of septic abortion, and two cases of local uterine puerperal infection, and one case of functional uterine bleeding treated with intrauterine penicillin. Two techniques are given, one continuous and the other intermittent. In both techniques a rubber catheter is sutured through the cervix. In the continuous method, 500,000 units of penicillin are diluted in 500 c.c. of normal saline and instilled in the uterus at the rate of 30 to 35 drops a minute. Approximately 2,000,000 units are given every 24 hours. In the intermittent method, the penicillin is instilled at three-hour intervals. The author has shown that penicillin is absorbed from the uterine cavity and produces effective bacteriostatic levels in the blood stream. It is suggested that this method might be used prophylactically and also might be of advantage in combating anaerobic streptococcus infection and infections with the *Clostridium welchii*.

L. M. HELLMAN.

Cancer, Malignancies

Marks, Joseph H., and Wittenborg, Martin H.: Results of Treatment of Carcinoma of the Ovary With Data on Age, Incidence of This Disease, Surg., Gynec. and Obst., page 541, Nov., 1948.

The authors report a series of 76 patients with carcinoma of the ovary, 57 of whom were followed until death. Fourteen showed a five-year survival rate. Although not all the patients had an opportunity to live five years, the calculated five-year survival rate was 21 per cent. The authors believe that surgery for carcinoma of the ovary should

be accompanied by x-ray therapy in all cases. They state that it is excellent insurance postoperatively. It may occasionally result in a cure even in advanced stages of the disease. The authors believe that the surgeon should not risk the patient's life with too meticulous removal of the carcinoma but that he should remove the easily accessible masses and then rely on x-ray. They state that x-ray therapy may bring gratifying relief even when cure is not achieved. The age, specific incidence in 494 cases of carcinoma of the ovary is shown. There was a definite decrease in the incidence of this type of carcinoma after the sixth decade. It, therefore, differed radically from other types of malignant tumor, which show an increase in incidence with age. L. M. HELLMAN.

Sicard, Andre: The Frequency of Ovarian Metastases From Carcinoma of the Breast, Presse Med. **56:** 606, Sept. 4, 1948.

The author, after reviewing 38 cases of breast carcinoma as related to surgical castration to control hormonal influence of the ovaries upon breast neoplastic metastases, found these observations after dividing his series into two groups: (1) In a subgroup of 23 women submitting to mastectomy, he discovered in two women microscopic ovarian metastases upon removal of the ovaries, an incidence of 11.0 per cent. In all instances the patients presented no clinical evidence of metastases. (2) In a second group of 15 women having obvious bone, nerve, or organ metastases, early or late, following mastectomy, he found ovarian metastases in nine cases, an incidence of 60.0 per cent.

Sicard concludes that surgical castration is, therefore, indicated after mastectomy for carcinoma of the breast if one would control metastasis. He found radiotherapy inadequate. CLAIR E. FOLSOME.

Emge, Ludwig A.: Six Cases of Primary Carcinoma of the Fallopian Tube, West. J. Surg. **56:** 334, June, 1948.

Six cases of primary carcinoma of the tube are reported among tubes removed from 2,000 patients, an incidence of 0.3 per cent. The vagaries of symptomatic manifestations obscure preoperative diagnosis to such a degree that early recognition of tumor is impossible. The author admits that he has nothing new to offer which might aid in early diagnosis, but he does emphasize the need for surgical exploration of obscure pelvic lesions when seen during the fifth and sixth decades of life. The more universal employment of the Papanicolaou smear and the more frequent use of hysterosalpingography may offer something for the future. WILLIAM BICKERS.

Acosta-Sison, H.: Dangers of Myometrial Chorionepithelioma Caused by Failure of Early Diagnosis, Philippine J. Surg. **2:** 240, Nov.-Dec., 1947.

Chorionepithelioma originating in the myometrium, without an endometrial focus, is most difficult to recognize clinically. Uterine bleeding is apt to be mild and delayed and curettement does not retrieve tumor tissue. Recognition thus disguised, the growth extends toward the uterine serosa. Intraperitoneal hemorrhage may force a diagnostic laparotomy.

Of 46 cases of chorionepithelioma admitted to the Philippine General Hospital in three years, eight were primary in the myometrium. In five of these, abnormal bleeding did not appear until 14 to 36 months after expulsion of the conceptus. In the one case so tested, the Friedman reaction was negative.

In addition to pregnancy gonadotropin titration, the author recommends his "HBEs method" for diagnosis. This is (H) a history of expulsion of an abortus, a term pregnancy, or a mole, (B) uterine bleeding, and (1) enlargement and softening of the corpus uteri. Unless there is a current abortion, this syndrome may signify a myometrial chorionepithelioma. IRVING L. FRANK.

Savran, J., Sayer, E. A., and Schradiak, C. E.: Primary Malignant Melanoma of Female Urethra, Am. J. Surg., page 743, May, 1948.

The authors briefly review the literature of the fourteen reported cases with this lesion and add one of their own. This reported melanoma was treated by local excision and her course was one of steady decline until her expiration 19 months later. No autopsy was performed. S. B. GUSBERG.

Cesarean Section

Ritala, A. M.: A New Modification of the Technique of Cesarean Section, Acta obst. et gynec. Scandinav. **26:** 604-609, 1946.

The author presents, with aid of eight drawings and four photographs, a modification of cesarean section. He utilizes the round ligaments to peritonealize and strengthen his repair of the uterine incision. Ritala contends this method offers two advantages: (1) prevention of scar in subsequent pregnancy, and (2) correction of uterus to normal anteflexed position. CLAIR E. FOLSOME.

Perez, Manuel Luis, and Echevarria, Ramon: Intraperitoneal Sulfonamide Prophylactic Treatment and Penicillin Therapy in Potentially Infected Cesarean Sections, Rev. obst. y ginec. **7:** 166-197, 1947.

The authors collect several series of cesarean sections treated with intraperitoneal sulfonamides and penicillin therapy. Twenty-six cases were from the T. De Alvear Maternity Hospital; eight cases from the senior author's private practice; nine cases from the junior author's private practice and twenty-six cases from the private practices of Drs. de la Colina, Rosenvasser, and Monti.

In all sixty cases the patients received 4 to 6 Gm. of sulfonamide powder intraperitoneally at time of the section. In several instances the sulfonamide dusting included application of it into the uterine cavity and wound. With but few exceptions, the patients received, in addition, doses of 20,000 Oxford Units of penicillin every 3 to 4 hours for an average total range of 400,000 to 600,000 units. In a few instances as much as 1,000,000 O. U. were used. Only eight of the sixty cases showed any untoward febrile response. One death occurred in the clinic series. Three patients had delayed hospitalization because of pelvic thrombophlebitis. The majority of the cases left the hospital in 10 to 12 days, some as early as the seventh day and one on the twentieth day. In the fatal case, the patient died of a postoperative accident (fecal fistula and peritonitis) 37 days after her section.

In all 60 instances, the patients gave histories of intrapartum obstetrical complications which would classify them as potentially infected cases. The authors conclude that the simple use of local intraperitoneal sulfonamides with subsequent penicillin therapy is adequate and less hazardous than specialized cesarean section operations.

CLAIR E. FOLSOME.

deCarle, Donald W., and Durfee, Raphael B.: The Pfannenstiel Incision for Cesarean Section, West. J. Surg. **56:** 360, June, 1948.

Sixty-one cesarean sections have been reviewed from the standpoint of the advantages and the disadvantages of the Pfannenstiel incision. Observations here reported would indicate that the transverse incision is associated with less discomfort and is therefore conducive to early ambulation. When using spinal or caudal anesthesia, a much lower level of anesthesia can be used, sparing the patient the hazard associated with large doses of anesthetic agent. The incision gives adequate exposure for delivery. The cosmetic advantage of this incision especially in the salubrious climate of California whence this article appears may be worthy of mention. WILLIAM BICKERS.

Endocrinology

Ziskin, Daniel E., and Moulton, Ruth: A Comparison of Oral and Vaginal Epithelial Smears, J. Clin. Endocrinol. **8:** 146, Feb., 1948.

In this study, the authors show that the changes that take place in the vaginal epithelial smears as a result of hormonal influence are, in part, reflected in oral epithelial smears. The obvious advantage of oral smears over vaginal smears, insofar as the ease of securing them and the emotional reaction of the patient are concerned, is pointed out.

Preliminary studies were carried out on rhesus monkeys. Oral and vaginal smears on a series of 23 women were compared. This group was composed of one girl with secondary amenorrhea, five women who had normal menstrual cycles, ten who were menopausal and had oral complaints such as burning or dryness of the mouth, and seven without oral complaints. From their studies the authors conclude that in the vaginal smear slight hormonal changes are more readily discernible than in the oral smear. The estrogenic response is more clearly demonstrated in the vaginal smear. The ovulation time can be more accurately predicted by the vaginal smear. Finally, in spite of the relative ease with which specimens can be obtained, the oral smear cannot replace the vaginal smear as a method of determining hormone levels in women. HERBERT J. SIMON.

Stewart, H. L., Jr., Sano, Machteld E., and Montgomery, Thaddeus L.: Hormone Secretion by Human Placenta Grown in Tissue Culture, J. Clin. Endocrinol. **8:** 175, Feb., 1948.

In this communication the authors offer experimental evidence in answer to the question as to whether or not the placenta is an organ of internal secretion. They grew human placenta in tissue culture and, from the tissue culture washings, biologic hormone titrations were carried out.

From the evidence presented in this paper, it would appear that the Langhans' cells of the placenta produce gonadotropin. It may be further predicated that the syncytial cells produce the estrogen. These hypotheses are substantiated by the fact that human placental tissue cultures result in rapid growth of the Langhans' cells and a corresponding increase in the hormone titrations for the gonadotropins; however, at the same time, the syncytial cells quickly disappear and repeated estrogen determinations fail to reveal its presence. Attempts were made to grow more mature placenta in culture, but were unsuccessful as fibroblasts soon overgrew the culture and there was no syncytial or Langhans' cell growth. HERBERT J. SIMON.

Eidelsberg, Joseph: Estrogens in Urine and Cytology of Vaginal Smears After the Use of an Estrogenic Cream, Am. J. M. Sc. **214:** 630, 1947.

In this study an effort was made to establish any demonstrable effect on the estrogen content of the urine and on the cytology of the vaginal smears after the use of an estrogenic cream which contained 7,500 International Units per ounce. The patients were instructed to apply approximately 1/14 of an ounce of the cream to the skin of the face each evening. Thus, about 535 International Units were used daily by the patients. Following proper control studies, the authors were unable to demonstrate any significant fluctuation in the urinary estrogen excretion, or any changes in the cytologic cycles of the vaginal smears. From this they conclude that the use of cream containing 535 International Units of estrogenic substance produces no systemic effect. HERBERT J. SIMON.

Menstruation, Dysmenorrhea

Usandizaga, Manuel: A General Concept and Nomenclature on Menstrual Disorders, Tokoginec. prát. **7:** 263-303, June, 1948.

The subject of a more acceptable classification of menstrual disorders had arisen at the First Spanish-Portuguese Congress of Obstetrics and Gynecology. Professor Usandizaga of Santander, Spain, offers a most scholarly paper with detailed explanations underlying the

placement of each disorder into its proper category. After defining normal menstruation and excluding many of the more frequently used adjectives, he finally arrives at a simple six-point classification. These points are given in the following outlined summary:

I. Abnormalities in relation to the onset or termination phases of menstruation:
   1. Abnormalities of the menarche: (a) precocious menarche; (b) late menarche.
   2. Abnormalities of the menopause: (a) precocious menopause; (b) late menopause.
   3. Castration: (a) operative castration; (b) radiological castration.

II. Absence of the periods:
   1. Amenorrhea; 2. cryptomenorrhea—hidden menses.

III. Abnormal periods with the chief disturbance in rhythm:
   1. Abnormalities in duration of cycle: (a) polymenorrhea; (b) oligomenorrhea.
   2. Abnormalities in volume of bleeding: (a) menorrhagias; (b) hypomenorrhea.

IV. Arrhythmic periods.

V. Hemorrhages in relation to the cycle but not appearing at catamenia:
   1. Slightly before the flow.
   2. Immediately after the period.
   3. In the intermenstrual period.
   4. Throughout the entire cycle.

VI. Phenomena which accompany the cycle:
   1. Premenstrual tension.
   2. Dysmenorrhea: (a) algomenorrhea (colicky abdominal or sacral pain); (b) menstrual molimina.
   3. Intermenstrual pain.

The author considers the entities of metropathia hemorrhagica, persistent corpus luteum cysts, and genital infantilism so well established they should be classed separately. He recommends further that we abandon such terms as ovarian insufficiency, hyper- and hypoestrination, functional hemorrhages, and also such adjectives as dysfunctional, pubertal, juvenile, and menopausal before the noun hemorrhage.

The author does use terms infrequently used in the States, but which aptly describe certain symptoms, viz.: (a) *algomenorrhea,* painful menses of colicky type; (2) *spanomenorrhea,* infrequent and scanty flows; (3) *eumenorrhea,* consistently normal periods; (4) *opsomenorrhea,* tardy menstrual periods, and (5) *proiomenorrhea,* premature menstrual flows.

The article is unusually well organized and based upon an excellently documented bibliography of 104 titles. CLAIR E. FOLSOME.

Ingersoll, Francis M., and Meigs, Joe V.: Presacral Neurectomy for Dysmenorrhea, New England J. Med. **238:** 357, March 11, 1948.

This paper deals with a series of presacral neurectomies performed for relief of dysmenorrhea. A total of 111 operations have been done at the Massachusetts General Hospital and the Palmer Memorial Hospital from 1930 to 1946. In most cases the neurectomy was combined with dilatation and curettage, a suspension, and any other necessary pelvic surgery that the gynecologic situation demanded.

By essential dysmenorrhea is meant painful menstruation that severely upsets the social and economic life of the patient; physical examination being negative. There were 89 such cases. In the acquired dysmenorrhea group there were nineteen cases, with sufficient pelvic pathology present to explain their dysmenorrhea.

The authors state that previous reports have adequately demonstrated the efficacy of presacral neurectomy in essential dysmenorrhea, which is now a standard operative procedure in pelvic surgery. They report in this series that complete relief was obtained in 81 per cent of essential and 52.6 per cent of acquired dysmenorrhea. There were twelve failures after presacral neurectomy for essential dysmenorrhea. These failures are accounted for on the basis of either regeneration of sympathetic nerves, incomplete operation, or dysmenorrhea as a manifestation of a psychoneurosis. Twenty-four women had babies postoperatively; labor was painless for 33.3 per cent. JAMES P. MARR.

Cadarso, J. R., De Guevara, L., and Strecht-Ribeiro, C.: Considerations Upon the Presacral Nerve in Dysmenorrhea, Rev. españ. obst. y ginec. 5: 1-12, Feb., 1948.

The authors obtained the specimens of resected presacral nerves from fourteen patients treated by this method for relief of dysmenorrhea, operated upon at Oporto Medical School. The specimens were fixed in 10 per cent formaldehyde or Bouin's solutions and stained with numerous stains including van Gieson, trichrome method of Masson, hematoxylin and eosin and special silver stains.

Among the pathological findings were congestion, perineural edema, perineural sclerosis, and intrafascicular sclerosis. They describe and illustrate pseudoneuronophagia, with nuclear degenerative changes: pyknosis, karyolysis, and alterations in the medullary fibers along with changes in the glial tissue (schwannosis, hyperplastic capsules) are the principal evidence of a predominant inflammatory change. More correctly, the pathological diagnosis of these resected nerves might be discrete neuroganglionitis. Six microphotographs are included.

CLAIR E. FOLSOME.

Miscellaneous

Oeconomos, Nicolas: Vaginal Wounds During Coitus, Gynec. et obst. 46: 557-563, 1948.

The author reports on three cases of women with vaginal wounds induced during intercourse who were seen at the Hotel-Dieu, Paris, on the surgical service of Pierre Brocq. The women were 39, 29, and 55 years old, respectively. The first of these cases suffered severe hemorrhages and it required total hysterectomy to control the two-franc size laceration to the left of the cul-de-sac. The other two cases also had the vaginal wounds on the left wall and fornix. Each of the latter was controlled by tamponage and local repair. In the case of the 55-year-old patient, there had been little sexual exposure after an earlier subtotal hysterectomy for fibroids.

The author gives considerable detail on the literature concerning this subject which in clinical practice is dramatic and requires rapid treatment. CLAIR E. FOLSOME.

DeLa Vega, J. C.: A Biological Pregnancy Test With Blood Obtained by Puncture of a Pelvic Hematoma, Bol. Soc. de obst. y ginec. de Buenos Aires 26: 98-102, Nov. 21, 1946.

The author reports on seven patients, most of whom gave an earlier history of acute abdominal pain, from whom he obtained blood via puncture of the cul-de-sac. In three cases, the Friedman or Hofman pregnancy tests were negative while in the remainder the tests were positive. He concludes the use of blood obtained from the cul-de-sac in these delayed, noncritical cases offers an important diagnostic aid when used in the biological tests.

CLAIR E. FOLSOME.

Udaondo, C. B., and Castex, M. R.: Bony Changes in Gastrectomized Patients, Presse méd. 55: 847-848, Dec. 20, 1947.

In view of the knowledge that gastric secretions contain an indispensable factor essential to the absorption of calcium and phosphorus into the intestine, the authors review 41 patients who had submitted to gastrectomy. Thirty-eight of this series had had stomach resection for gastroduodenal ulcers, two cases for carcinoma of the stomach, and one case for sarcoma. The patients' ages varied between 24 and 67 years. Thirty-four were men and seven were women. Radiologic studies indicated that 95.12 per cent of the series showed some decalcification of their lumbosacral spine or pelvic bones. The degree of decalcification varied as follows: small amount, 17.0 per cent; discrete areas in 41.4 per cent; moderate decalcification in 29.25 per cent; and heavy losses in 7.31 per cent. In 60 per cent of the series of 26 patients upon whom inorganic phosphorus and calcium determinations of the

serum and plasma alkaline phophatase activity values were made, a normal calcemia was found but all in lower normal limits. All of these cases showed a normal phosphatemia or a slight elevation.

The authors conclude that the decalcification of the lumbosacral and pelvic bones in gastrectomized patients is extremely important. Clinicians must, therefore, consider supplemental therapy in such cases and recognize that other gastric disturbances may cause serious bony changes. Prevention with proper medication may preclude such bony changes.

CLAIR E. FOLSOME.

Mack, Harold C., Parks, A. E., and McDonald, Marian: Further Observations on the Pregnandiol Test, Harper Hosp. Bull. 6: 33, 1948.

A test for pregnandiol in the urine depending upon the precipitation of unpurified pregnandiol has previously been described; the technique is again described in this article. With this simplified test, the findings closely parallel those obtained with the more elaborate quantitative methods. In normal menstrual cycles, in which the excretion of pregnandiol was correlated with the basal body temperature curve, it was found that excretion of pregnandiol followed the postovulatory rise in temperature. In one case in which a planned pregnancy followed ovulation, temperature levels were sustained and pregnandiol excretion continued, as is typical of normal pregnancy. In cases with irregular cycles, with delayed ovulation, pregnandiol excretion also occurs late in the cycle.

The pregnandiol precipitation test has been employed in conjunction with the Friedman test for all specimens submitted for the diagnosis of pregnancy. In 306 urine samples, from patients subsequently found to be pregnant, positive pregnandiol tests indicated a diagnosis of pregnancy correctly in 291 instances (95.1 per cent); there were 15 incorrect negative diagnoses (4.9 per cent). The Friedman test on 280 of these urines gave a correct positive diagnosis of pregnancy in 268 cases (95.7 per cent) and a false negative in 12 cases (4.3 per cent). In 275 urine samples from patients who were subsequently found not to be pregnant, the pregnandiol test was negative in 245 (or 89.1 per cent), and falsely positive in thirty, (or 11.9 per cent). For these same urines the Friedman test gave only 4 false positives. In ten of the thirty cases in which the pregnandiol test gave a false positive, no data on the clinical history were available; in twelve cases there was no amenorrhea; in six cases the menstrual cycle was irregular; one patient was lactating; and one had a corpus luteum cyst. It is evident that the pregnandiol test gives presumptive evidence of pregnancy only if the urine is obtained in a period of amenorrhea in women whose menstrual cycles are otherwise normal. If the cycle is longer than the usual twenty-eight days, late pregnandiol excretion is to be expected because of late ovulation.

The pregnandiol test was also employed in 105 patients with symptoms of threatened abortion in the early months of pregnancy. In 39 cases the pregnandiol test was negative when the patient was first seen or became negative during the period of observation, and abortion occurred in all but two of these cases. In 54 cases in which the pregnandiol test remained positive, abortion did not occur, but in twelve cases with positive pregnandiol tests, abortion did occur. The prognostic value of the qualitative pregnandiol test in threatened abortion is greatest in the first three months of pregnancy. After that time increasing placental function increases the output of pregnandiol and a quantitative test is necessary to determine if there is a diminished progesterone metabolism. HARVEY B. MATTHEWS.

Riley, Gardner M., Smith, Marjorie H., and Brown, Pearl: The Rapid Rat Test for Pregnancy, J. Clin. Endocrinol. 8: 233, March, 1948.

The authors review reports in the literature on the rapid rat test for pregnancy. The test is based on the hyperemic response in the ovaries of immature rats as a result of the injection of pregnancy urine.

The comparative results are given, using this test and simultaneously the conventional Aschheim-Zondek test on the same urine. In addition, the hyperemic response elicited under various known experimental conditions is described. From these experiments, they deduced that it is best to allow four to six hours to elapse between injection and sacrifice of the animals, though there appeared to be no advantage to lengthening the interval to sixteen hours.

The strongest hyperemic response was obtained most uniformly in the heavier test animals (weighing 55 to 70 Gm.). This study demonstrated the desirability of establishing the responsiveness or refractoriness to chorionic gonadotropin. The authors chose albino rats of the Wistar strain.

Attention is called to the fact that, in cases of disturbed pregnancy such as threatened or incomplete abortion or ectopic pregnancy, where an intermediate type of response in the Aschheim-Zondek test is found, the hyperemia test is of little diagnostic value. However, the rapidity and simplicity of the test, together with its high degree of accuracy, in cases of normal pregnancy, make it a valuable diagnostic procedure. HERBERT J. SIMON.

Newborn

Ware, H. Hudnall, Jr.: Abnormal Presentation, J. A. M. A. **137:** 448, May 29, 1948.

The author reviews the various types of abnormal presentation and discusses the treatment of each. Throughout the discussion the author stresses the importance of pelvic measurements prior to the onset of labor, and a careful estimate of the fetal size, especially the fetal head. WILLIAM BERMAN.

Nielson, Harriet K., Ferris, Deward O., and Logan, George B.: Injury of the Penis, Scrotum and Buttocks of the Newborn Resulting in Gangrene, Am. J. Dis. Child. **75:** 85, Jan., 1948.

The case report from the Division of Surgery and the Section of Pediatrics of the Mayo Clinic concerns a multipara who after a twenty-four hour labor delivered herself of a male child with a breech presentation. At the time of delivery the scrotum was estimated the size of a grapefruit and the penis to be red and about four times normal size.

Twenty-four hours later the baby was admitted to the hospital. A support was applied to the scrotum. Penicillin, in doses of 5,000 units, was given intramuscularly every three hours for thirty-nine days. Lines demarcating the gangrenous lesion formed on the penis, scrotum, and buttocks on the fourth day. On the sixteenth day, gangrenous material was removed and the testes exposed and examined.

Primary skin grafting could not be carried out because of infection. Therefore, granulation and epithelization were encouraged in order to bring together the edges of the remaining part of the scrotum.

The patient returned to the clinic one year later, at which time the left testis seemed small and fibrotic. The right testis seemed about normal in size.

Photographs are inclosed showing the preoperative condition and the postoperative results. JAMES P. MARR.

Franklin, H. Charles, With the Technical Assistance of Loeb, Laura N.: Bacterial Flora in Eyes of Newborn Infants During First Forty Hours of Life—After Single Instillation of Penicillin and Silver Nitrate, J. Pediat. **32:** 251, March, 1948.

This report is from the Department of Obstetrics and Gynecology at the University of Tennessee College of Medicine. The study treats of the bacterial flora in the eyes of 200 infants during the first forty hours of life. One hundred were studied after prophylaxis employing a single instillation of penicillin, and 100 after a single instillation of silver nitrate.

This study indicates by bacteriologic findings that penicillin, when used as a single instillation, compares favorably with silver nitrate as a prophylactic agent. (41 per cent positive cultures after penicillin and 45 per cent positive cultures after silver nitrate.)

Further study is required for interpretation of the observed increase of the bacterial flora with time in the conjunctiva of the newborn infant. JAMES P. MARR.

Rutherford, Frederick W.: Recent Advances in Surgery of the Newborn and of Early Infancy, West. J. Surg., page 298, May, 1948.

Peculiar metabolic requirements and the high surgical incidence of embryonic malformations make the surgery of the newborn and the infant a distinct specialty. Cleft lip and palate is best repaired during the period of maximum immunity in the first few weeks of life. Surgical repair of the palate may be deferred for twelve months. Attention should be given to dentition, care being used to protect the unerupted teeth. Adequate speech training is a necessary counterpart to surgery.

Tracheo-esophageal fistula is suspected when choking, coughing, and gasping occur of the time of the first feeding. Adequate parenteral fluid is given, cyclopropane by intubation for anesthesia, and primary anastomosis is usually possible. Peptic ulcer, usually the duodenal type, is fairly common and hemorrhage or perforation demands immediate operation. Congenital hypertrophic pyloric stenosis should no longer be considered an indication for emergency surgery, but a few days spent in re-establishing the electrolyte, fluid, protein, and vitamin balance is time well spent. Congenital atresia of the intestine or colon is characterized by delayed vomiting, and Lipiodol x-ray, never barium, is helpful. Preoperative preparation with duodenal suction and postoperative feedings with fat-free protein milk hasten recovery. Several anomalies of the anus and rectum are readily diagnosed and usually lend themselves readily to surgical correction. Intussusception sometime presents difficulty in diagnosis, but the infant previously healthy who has sudden abdominal pain, bloody stool, and a palpable abdominal tumor demands immediate operation. Congenital atresia of the bile duct is suspected when jaundice is progressive. Umbilical eventration and congenital diaphragmatic hernia are major procedures which cannot long be delayed. WILLIAM BICKERS.

Toxemia

Garber, Stanley T., and Assali, N. S.: Toxemias of Pregnancy, An. brasil. de gynec. 25: 87-100, Feb., 1948.

The authors review 1,310 cases of toxemia of pregnancy treated at the Cincinnati General Hospital over a six-year period, 1940 to 1945 inclusive. They classify their cases as 680 mild cases of toxemia; 379 severe toxemias; 40 instances of eclampsia, and 211 cases of hypertensive disease in pregnancy. During this time interval, six years, 13,784 deliveries were performed in this hospital, thus giving an incidence of 10 per cent toxemias of pregnancy. There were four maternal deaths, three in the pre-eclamptic group (0.8 per cent), and one death among the 40 eclampsia cases (2.4 per cent). There were 130 infant deaths in the series, which included 41 premature and 46 term stillborn infants and 24 premature and 19 term neonatal deaths. There were fifteen abortions in the series. The infant mortality as uncorrected was found to be 9.8 per cent and the uncorrected maternal mortality rate was 0.3 per cent.

The treatment stressed rest, salt-poor diet, magnesium sulfate, hypertonic glucose solutions and veratrum viride along with forced fluids and proper sedation. Three tables are included. CLAIR E. FOLSOME.

Leon, Juan: Toxemia of Pregnancy, Anales del Servicio de Obstetricia del Hospital Cosme Argerich 1: 25-41, Dec., 1947.

The author, of Buenos Aires, does not subscribe to the theory that the so-called toxemias of pregnancy are due to toxic substances or are of ovular origin. He feels that the progress

achieved in the biophysiochemical domain permits another possible explanation for the cause of toxemias of pregnancy. In normal pregnancy there exists a peculiar state of equilibrium differing fundamentally, but in a state of perfect adaptation, from the nonpregnant state. In the so-called toxemias there exists a singularly unstable neurovegetative glandular, ionic, and colloidal state of biophysiochemical balances.

The writer proposes a new term, *Gravid, psychosomatic unstable equilibrium.* Instead of the American Welfare Committee of Maternity's usually accepted classification, he proposes regrouping the toxemias as (a) convulsive; (2) comatose; (3) hemorrhagic; (4) bilateral cortical necrosis of the kidneys; and (5) pyelitis of pregnancy.

The author then concludes with considerable detail on the physicochemical findings of blood. These he attempts to use to show the great influence of the mind upon functional disturbances and morphological variations often seen in pregnancy. Another term used instead of toxemia is *Psycho-organic Imbalance.* CLAIR E. FOLSOME.

Peet, Max M., Isberg, Emil M., and Bassett, Robert C.: Toxemia Superimposed Upon Prepregnant Hypertension Treated by Splanchnicectomy, Surg., Gynec. & Obst., 1948.

The authors present the histories of five patients with severe chronic hypertensive vascular disease complicating pregnancy. They state that the patients were also suffering from superimposed toxemia but this does not seem probable either from examination of the histories or from the duration of the pregnancies, all of which were five months or less. The patients received bilateral supradiaphragmatic splanchnicectomy with lower dorsal sympathetic ganglionectomy. In two of these the results were excellent, normal blood pressure levels being achieved, living children obtained, and a persistent cure of the hypertension effected. In the remaining three the hypertension was not relieved during the pregnancy, although in one there has been a subsequent diminution in pressure. L. M. HELLMAN.

Correspondence

Abdominal Cystoceleoplasty

To the Editor:

In his presidential address to the American Gynecological Society in 1912, Howard A. Kelly began, "According as we remember others, so those yet to come will remember us." With this in mind, I cannot refrain from calling attention to the fact that, in that year of 1912, Dr. William Mecklenberg Polk read a paper at a meeting of the American Gynecological Society, noted in the Society's Transactions (*American Journal of Obstetrics and Diseases of Women and Children,* vol. 66, page 639) entitled "Procidentia Uteri: Suprapubic Plication of Vagina and Conjoined Shortening of Uterosacral and Broad Ligaments." This address presented the same technique that Dr. Charles B. Marek publishes in your JOURNAL, February, 1949, on page 345.

In addition, in the September number of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY of 1929, page 345, I published an article entitled, "Intra-abdominal Reefing of the Pubocervical Fascia (Modified Polk Operation) for the Cure of Cystocèle," in which I sought to revive the then obsolete Polk operation, applying it to cases in which supravaginal hysterectomy or ventrofixation was employed.

In retrospect, I may say that I have again abandoned the operation because recurrence of cystocele eventually took place in a considerable number of cases.

ROBERT T. FRANK, M.D.

1035 PARK AVENUE
NEW YORK CITY
March 11, 1949

Item

First Mexican Congress of Gynecology and Obstetrics

May 22–May 28, 1949, Mexico City, Mexico

The Mexican Gynecological and Obstetrical Association and its Affiliated Societies have organized the First Mexican Congress of Gynecology and Obstetrics, which will take place in Mexico City from May 22 to May 28, 1949. The scientific papers will be presented in the "Justo Sierra" (U.N.E.S.C.O.) Auditorium of the Escuela Normal de Maestros, and the social reunions in the Hotel del Prado. There will also be visits to the hospitals and clinics of the city and there will be ceremonies at the Chapultepec Castle and the Palace of Fine Arts, etc.

Any further information will be furnished by the Secretary of the Congress, Dr. Carlos Guerrera, Marsella 11, Mexico City.

Necrology

FRANKLIN S. NEWELL, A.B., M.D., professor emeritus of clinical obstetrics at Harvard Medical School, died on March 3, 1949, in Boston, at the age of 77 years. A native of Roxbury, Massachusetts, he received his B.A. in 1892, and an M.D. in 1896, both at Harvard. He became visiting obstetrician to the Boston Lying-In Hospital in 1899, and served until his retirement in 1931. Dr. Newell was appointed in 1897 as assistant professor of obstetrics and gynecology at Harvard and then became full professor in 1917, until his retirement in 1931.

A frequent contributor to the JOURNAL, Dr. Newell was co-author with Dr. Edward Reynolds of a textbook on "Practical Obstetrics." President of the American Gynecological Society in 1926, he was also a member of the Boston Obstetrical Society and other medical organizations.

HOWARD CANNING TAYLOR, PH.B., M.D., well-known gynecologist of New York City, died at his home March 27, 1949, at the age of 82 years. Born in Greenes Farms, Conn., he graduated at Yale in 1888 and from the College of Physicians and Surgeons of New York in 1891. Dr. Taylor was affiliated with the Roosevelt Hospital during his entire professional life, beginning as an intern, then as attending gynecologist, and finally as consultant. He was also a clinical professor at the College from which he graduated. A Fellow of the New York Obstetrical Society and the American Gynecological Society, he had served as president of both organizations. Dr. Taylor was a member for many years of the Advisory Editorial Board of this JOURNAL and on his retirement was succeeded by his son, now an Associate Editor.

CONTENTS FOR JUNE, 1949

Transactions of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons

Fifty-Ninth Annual Meeting, Hot Springs, Va., Sept. 9, 10, 11, 1948

Presidential Address. Nutrition and Human Reproduction: An Historical Review. Robert D. Mussey, M.D., Rochester, Minn. ---- 1037

Medicine's Response to the Challenge of Our Time. Raymond Bernard Allen, M.D., Seattle, Wash. President, University of Washington ---------- 1049

A Survey of 113 Cases of Primary Dysmenorrhea Treated by Neurectomy. O'Donel Browne, Litt. D., M.B., M.A., M.A.O., F.R.C.P.I., F.R.C.O.G., Master, The Rotunda Hospital, Dublin; King's Professor of Midwifery, Trinity College, Dublin ---------- 1053

Operative Procedures for the Treatment of Sterility and Ovarian Dysfunctions. James L. Reycraft, M.A., M.D., Cleveland, Ohio ---- 1069

A Study and Classification of Pelvic Inflammatory Disease. Roy W. Mohler, M.D., Sc.D., Philadelphia, Pa. ---------- 1077

Retroperitoneal Lymph Node Dissection in Cancer of the Cervix. Joe Vincent Meigs, M.D., Langdon Parsons, M.D., and Ira T. Nathanson, M.D., Boston, Mass. ---------- 1087

An Attack Upon the Delay Period in Diagnosis of Pelvic Cancer. John Y. Howson, M.D., and Thaddeus L. Montgomery, M.D., Philadelphia, Pa. ---------- 1098

Clinical and Pathological Studies of Feminizing Tumors of the Ovary. Frederick H. Falls, M.S., M.D., F.A.C.S., Alex B. Ragins, M.S., M.D., and Morris Goldenberg, M.D., Chicago, Ill. ---------- 1107

Nonneoplastic Ovarian Cysts; Their Relation to Spiral Arteries in the Human Ovary. Barnet Delson, B.S., M.D., Brooklyn, N. Y. -- 1120

The Early Diagnosis of Carcinoma of the Cervix With Emphasis on Routine Biopsy. Frank R. Lock, A.B., M.D., and Jesse B. Caldwell, B.S., M.D., C.M., Winston-Salem, N. C. ---------- 1133

Ectopic Pregnancy, Mortality and Morbidity Factors. Conrad G. Collins, M.D., Woodard D. Beacham, M.D., and Dan W. Beacham, M.D., New Orleans, La. ---------- 1144

(Continued on page 8)

FOR INTENSIVE THERAPY...

HIGH POTENCY CHORIONIC GONADOTROPIN

"A.P.L."®

Brand of Chorionic Gonadotropin

There is reason to believe that, in certain cases, more favorable results may be obtained with doses of "A.P.L." larger than those heretofore recommended.[1] "A.P.L." No. 972, in dried form, is designed to facilitate the administration of massive dosages. Each package provides:

1. One "Secule" containing 20,000 I.U.*
2. One 10 cc. vial sterile diluent containing 0.5% phenol. "A.P.L." (Dried) may be reconstituted to a volume of 5 or 10 cc., thus providing concentrations of 4,000 or 2,000 I.U. per cc. "A.P.L." is also supplied in sterile solution as follows:
No. 500—500 I.U. per cc.—10 cc. vials
No. 999—1000 I.U. per cc.—10 cc. vials

"A.P.L." has been used successfully in the treatment of chronic cystic mastitis, threatened abortion, functional uterine bleeding, cryptorchidism, hypogenitalism, and Fröhlich's syndrome.

[1]Brown, W. E. & Bradbury, J.T.: Am. J. Obst. & Gynec. **53**:749 (May) 1947.

*"Secule"—Ayerst name to designate a special vial containing an injectable preparation in dried form.

4915

Ayerst, McKenna & Harrison Limited
22 East 40th Street, New York 16, N. Y.

CONTENTS (*Continued from page 6*)

Know the Pelvis. William T. Kennedy, M.B., F.A.C.S., New York, N. Y. ---------- 1155

A Report on the Cesarean Sections Done in St. Vincent's Hospital, New York. James P. Hennessy, M.D., F.A.C.S., New York, N. Y. ---------- 1167

The Role of Penicillin in Obstetrics. Capt. L. Marshall Harris (MC) USN, and Lt.(jg) Daniel M. Shook (MC)USN, Great Lakes, Ill. 1186

Continuous Spinal Anesthesia in Cesarean Section. Clifford B. Lull, M.D., and John C. Ullery, M.D., Philadelphia, Pa. ---------- 1199

Elderly Primigravid Women. Lawrence M. Randall, M.D., and John Champneys Taylor, M.D., Rochester, Minn. ---------- 1210

Index

Index ---------- 1223

American Journal of Obstetrics and Gynecology

Editor: GEORGE W. KOSMAK

Associate Editors: HOWARD C. TAYLOR, JR., and WILLIAM J. DIECKMANN